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ACTA PÆDIATRICA

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EXPERIMENTAL RICKETS

STUDIES IN RESPECT OF CALCIUM, PHOSPHORUS
AND MAGNESIUM METABOLISM

BY

T. SKAAR

Acta Pædiatrica. Vol. XII. Supplementum I

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To My Friend

Mr. Otto Börs

I dedicate this work.



The experimental investigations which form the basis of this work were undertaken at the Royal Norwegian University, Oslo, during the period 1925 to 1929.

To all who in any way assisted me during this period I wish to express my thanks.

The work has been carried out with the financial assistance of «A/S Freya chokoladefabriks medicinske fond», «Stadssekretær J. Aall og hustrus legat», and «Grosserer Thor Dahls legat», for which assistance I would extend my thanks to the Legacy Councils concerned.

Oslo: May 1931.

T. Skaar.

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1. Introduction.

It has long been established that both human rickets and experimental rickets give rise to changes, varying in degree, in mineral metabolism, especially calcium and phosphorus metabolism, and in this respect several investigators have published the results of their experiments.

The investigations carried out up to the present, however, have been conducted partly with a view to a single element only; further, they have, to some extent, been of short duration, and, in cases, the pathological and physiological conditions have not been controlled simultaneously.

The investigations, the results of which are set out herein, were accordingly undertaken with the object of studying the calcium and phosphorus metabolism of both normal and rickety puppies; further, to control constantly the relationship of these substances in the blood serum, and, finally, at the conclusion of the investigations, to examine the skeleton system chemically and microscopically. As it could be thought that metabolism during experimental rickets would be influenced not only by the lack of Vitamin D but also by the lack of Vitamin C, it was obvious in these investigations to combine the deficiency of the 2 Vitamins in the diet, as well as to exclude the one or the other, although no description of scurvy or scurvy-like conditions in dogs can be found as having been published.

2. Earlier Investigations.

There is no doubt that rickets was prevalent in ancient times and it is also possible that the physicians of those days, such as Hippokrates, Theodosius and others, have been aware of this infirm condition in children but they cannot be found to have given any proper, typical and exhaustive description of the disease.

When, at the beginning of the 17th century, rickets became very prevalent in various parts of England, FRANCIS GLISSON, in 1650, published his work: *De rachitide s. morb. puer. qui vulgo the rickets dicitur Tractatus*, in which he gives a detailed description of the clinical picture rickets presented. He describes the thickening of the epiphyses of the long-shafted bones, the deformity of the thorax, «rosary» corresponding to the thickening of the junction of rib and cartilage, the distended, prominent abdomen, weak musculature, and the poor condition generally of the individual afflicted. He considered that a cold climate and poor nourishment could give rise to the disease.

For a few centuries comparatively little mention was made of the disease. A few investigators, however, worked on the subject, but no great progress was made in identifying the disease until 1850, when R. VIRCHOW (1) separated osteomalacia from rickets and evidenced the histological picture presented by the latter.

As the most prominent symptoms of rickets are the changes in the skeleton, it was only natural that, when the study of the disease progressed more rapidly, most investigators devoted themselves histologically to the study of the deformities of the skeleton in the hope of thereby ascertaining the ætiological factors. The changes undergone by the bones have accordingly been carefully studied not only by VIRCHOW, but also by KASSOWITZ, MARFAN, v. RECKLINGHAUSEN, SCHMORL and POMMER. As all microscopical discoveries clearly revealed that there was, above all, a deficiency of lime deposition in the bones, it was soon realised that the main ailing changes in rickets were concerned with mineral metabolism and, even if the few decades immediately following gave several misleading and wrong theories, knowledge of the disease improved steadily. Of investigations proper of metabolism, there have not been so very many as attention was soon directed towards the effect of a single substance on the course of the disease, without, however, the metabolism of that element being examined.

G. WEGNER (1892) (2) studied the therapeutic effect of

the element phosphorus administered repeatedly in small doses, and he considers he achieved successful results by treating rickets in this manner. ROLOFF (1875—79) (3) supported him, maintaining that rickets is due to a lack of phosphorus in food.

As early as 1842, MARCHAND (4) advanced the theory that the lack of calcium-phosphate in the bones must be looked for in the increased amount of lactic acid in the organism due to the great fermentation of carbo-hydrates in the intestines. He also maintained that he could prove the presence of large quantities of lactic acid in the urine of rickety children. In his opinion, therefore, rickets was not originally a disease of the bones, but an illness arising from wrong digestion and poor nourishment. He considered that rickets could be resisted by giving substances not conducive to the formation of lactic acid, not milk, for example.

As long ago as 1844 and 1847, LIEBIG proved that lactic acid was not found in urine. HEITZMANN (1873) (5) believed that he had produced rickets and osteomalacia by giving a diet lacking CaO but with lactic acid added, whereas HEISS (1876) (6), concludes, that even by dosing a dog with large quantities of lactic acid, the presence of this acid in the urine cannot be proved, all lactic acid therefore being reduced and separated into its elements in the organism.

In 1880 E. VOIT (7) maintained the utility of dieting with calcium salt in cases of florid rickets and recommended that attention should be given to the gastro-intestic disturbances of the disease. He was of the opinion that these were the origin of the disease and that their removal would lead to its cure.

KASSOWITZ (1881—94) (8) also carried out experiments with phosphorus therapeutics in the case of rickets and he expressed the opinion that the disease is not due to a lack of CaO in diet. He found that phosphorus made the bones hard.

In 1882, OPPENHEIMER (9) came with his theory of «intermittens», but this was soon swept aside as the spreading of the disease alone was sufficient to disprove it.

POMMER (1885) (10), on the basis of the morphological changes produced by human rickets in the skeleton system,

sought to discover the origin and the original causes of the disease, but he was obliged to confine himself to saying that the cause-conditions of the rachitic bone disturbances lay outside the skeletal system.

CHABRIÉ (1894—95) (11) put forward the theory that rickets is due to the intervention of lactic acid in the normal development of collagen of chondrin, a process which is necessary for normal ossification, and also to the intervention of lactic acid by the normal precipitation of calcium phosphate and calcium carbonate in bone by the fixation of carbonic acid to lecithin. He considered that the lactic acid would keep it dissolved, and that lecithin would thus be necessary for the normal utilization of inorganic phosphorus. He also explained the partial replacement of calcium in the bones by magnesium in osteomalacia by referring to a varying relationship to lecithin. At about the same time PAROT says: «le rachitisme ne reconnaît pas d'autre cause que la syphilis héréditaire». VIERORDT (1896) (12), on the other hand, is more cautious as he merely maintains that syphilis predisposes rickets. PAROT's doctrine was speedily dropped and there remained only the pseudo-rachitic forms of hereditary syphilis which belong to the differential diagnosis of human rickets.

In 1899 DELCOURT (13) recorded that, by adding sodium phosphate to the diet, he had produced bone changes resembling those in rickets.

In 1900 ZWEIFEL (14) launched the theory that the lack of muriatic acid in the gastric juices which may arise owing to the lack of ordinary salt in food, prevented the calcium salts from dissolving, thus causing rickets by the direct lack of lime.

STOELTZNER (15) advances negative results of therapeutic phosphorus in cases of marked disease, recommends, moreover, that phosphorus should be given in cod-liver oil, and considers that a cause of rickets is a functional insufficiency in an organ analogous to the thyroid gland. He had maintained, somewhat earlier (16), that in rickets he had secured a good effect by dieting with a suprarenal gland substance. Moreover, rickets has been described as a disturbance of the function of the

suprarenal glands and such investigators as LANG and KNOEFFEL-MACHER (17) have also connected it with functional disturbances of other glands having internal secretion like the thyroid, parathyroid and thymus glands. BASCH (19) and MATTI (20), however, maintain that the removal of the thymus determines rickets, but this has been disproved by PARK and McCURE (21) as well as by others. So late as 1914 J. KOCH (22) was of the opinion that rickets can be produced by inoculation with bacteria. He considered that streptococcus longus was best at producing rickets, but, unfortunately, his control animal which was not inoculated with bacteria, developed rickets as well.

It was, however, more reasonable to connect the origin of the disease with the nourishment of the individual concerned and as early as 1906 HOPKINS (23) wrote: «But further, no animal can live upon a mixture of pure protein, fat and carbohydrate, and even when the necessary inorganic material is carefully supplied the animal still cannot flourish. Scurvy and rickets are conditions so severe that they force themselves upon our attention but many other nutritive errors affect the health of individuals to a degree most important to themselves and some of them depend upon unsuspected dietetic factors.»

The experiments HOPKINS made, mark the commencement of attention being drawn to the importance of «the accessory factors of the diet». After C. FUNK (24) had characterised these accessory food-substances with the name «Vitamins», MELLANBY (25) was the first to prove the presence of such an accessory factor in rickets which he termed the anti-rachitic vitamin, and no sooner had he proved that rickets could be produced by giving a diet poor in anti-rachitic vitamin, than investigations regarding rickets were conducted through a new channel. A considerable amount of work has since been undertaken to discover the aetiology of the disease.

In 1921 SHERMANN and PAPPENHEIMER (26) discovered that a diet containing small quantities of phosphorus caused rickets in rats and that rickets can again be counteracted by the addition of sodium phosphate to a diet poor in phosphorus. Later, works appeared by PAPPENHEIMER, McCANN and ZUCKER

(27) and McCOLLUM, SIMMONDS, SHIPLEY and PARK (28), proving the same, so that more attention was now given to the inorganic components, particularly phosphorus in the composition of the various rickets-producing diets. Experimental rickets can, accordingly, now be produced in rats by various methods when the diet given does not contain the anti-rachitic vitamin or the animals are not submitted to ultra-violet rays, which are also anti-rachitic. As McCOLLUM and his co-workers (28) have done under these conditions, the rats may be given a diet containing small quantities of phosphorus and large quantities of calcium carbonate, calcium lactate or calcium chloride. Rickets is then produced owing to the small quantities of inorganic phosphorus in the blood, with microscopical bone discoveries corresponding to human rickets as well; or, like PAPPENHEIMER (29) the quantity of calcium can be decreased and the quantity of phosphorus increased constantly higher than the amount of calcium in the diet. Further, experimental rickets, corresponding to rickets obtained by giving small quantities of phosphorus and large quantities of calcium in the diet, can be produced by adding magnesium carbonate to the diet. (McCOLLUM and PARK) (30). Finally, according to what McCOLLUM has discovered in rats which do not receive anti-rachitic vitamins or are not submitted to ultra-violet rays, the appearance of rickets can be countered by the composition of the salt mixture. McCOLLUM and his colleagues (30), moreover, have proved that the rachitic condition improves during hunger.

So far as actual investigation into metabolism is concerned, especially in respect of calcium and phosphorus, not much has been undertaken during the years under review. CRONHEIM and MÜLLER in 1908 were the first in this respect, but the rickety children they examined showed the same value of calcium and phosphorus retained, as normal children, and judging from these results, it would accordingly seem that the rickety children must have already reached a convalescent stage.

About the same time W. BIRK (31) discovered that the mineral metabolism of rickety children can be negative and that in such cases the phosphorus-cod-liver oil increases the calcium

and magnesium balances, while the retention of phosphorus remains uninfluenced by it. A little later BIER and ORGLER (32) found that in rickets the lime deposition, even before it is chemically manifest, is below the quantity necessary for a child.

In 1910, SCHABAD (33) came with important investigations regarding calcium, and later, also in respect of phosphorus metabolism in rickets. In fresh progressive rickets the balance of calcium is either negative or below normal. It is positive during convalescence but during development there is an increased excretion of phosphorus. But as no increased excretion of calcium is to be found in urine during the development of rickets and when rickets has developed, the acid theory with regard to the origin of the disease cannot be maintained. According to this theory of the origin of rickets, a large formation of acid should take place in the intestines, in particular of lactic acid from alimentary substances, a formation of acid which should either prevent resorption in the intestines or dissolve the calcium in the bones. This is a theory which is defended by HEITZMANN (34) and others, but, as stated, it is one which cannot be maintained in view of the circumstances discovered by SCHABAD. Further, SCHABAD finds that an increased excretion of calcium in faeces leads to retention of phosphorus in the intestines, and the reverse; and as he also maintains that during rickets more phosphorus than calcium is excreted, the possibility is excluded of linking the phosphorus excretion with an increased excretion of calcium. In his opinion the primary cause of the disturbances of metabolism is rather to be looked for in the increased phosphorus excretion. Finally, he found that, in cases of pronounced rickets, the bone ash is changed more in respect of phosphorus than of calcium, the normal relationship between Ca and P, which is 100:75—85 having fallen to 100:70—74 where the phosphorus is concerned.

ARON and SEBAUER (35) put the minimum value of the calcium requirement in the case of a growing dog at 1.2 % CaO of the increase in weight of the animal. As a cause of rickets, ARON, SCHABAD and DIBBELT, all maintain the lack

of calcium in nourishment. They base their opinions on investigations made with breast-fed children where, between supply and demand, an incompatibility exists, which, if the demand is as great as these investigations maintain, is 0.25 gm. CaO per 100 gm. increase in weight. If a similar demand, however, is presumed, as, for example, like ORGLER (36), viz., 0.17 gm. CaO, then the woman's milk, in most cases investigated, has been found to be sufficiently rich in CaO with no incompatibility arising between supply and demand.

KOCHMANN (37), on the contrary, maintains that it is impossible to give minimum values to maintain the even balance of calcium, as the necessary calcium depends upon the kind and quantity of the nourishment, as proteins, fats and carbohydrates influence the calcium balance.

The balance can be maintained and the calcium displaced by both soluble and dissoluble salts in the food. KOCHMANN finds, moreover, that the phosphorus metabolism is influenced both by calcium and by nitrogen metabolism. If the doses of phosphorus are to act on metabolism, the toxic quantities are arrived at without their showing any influence beyond the time they are given.

SCHABAD and ORGLER and others have examined the effect of various calcium salts administered per os. They show that a large supply of calcium during rickets is not able to counteract a negative balance, whereas during convalescence one is able in this manner to maintain the retention of calcium. They concluded from this that the organism in the advanced stage of rickets is not able to deposit calcium.

From tests made with growing dogs LIPSCHÜTZ (38) finds that a deposition of 0.144 gm. P per diem per kg. weight of body is normal, a calculation also given by HEUBNER (39).

If, however, metabolism in rickets has not previously been a matter for much investigation, the quantity of both calcium and phosphorus in the serum during rickets and its cure has been repeatedly examined. HESS and his co-workers (40) accordingly say: «Calcium may or may not be lowered», but the majority of investigators like KRAMER, TISDALL, and HOWLAND

(41) are agreed that in rickets a moderate lowering of the quantity of calcium in the serum is found. FABER (42) comes to the same conclusion, both in rickets and spasmophilia.

According to IVERSEN and LENSTRUP (43), HOWLAND and KRAMER (44) and FABER (42), all investigations regarding the quantity of phosphorus in the serum proceed on the assumption that this is lowered by rickets.

On the other hand, HESS and UNGER (40) maintain that there are also some cases of rickets where the phosphorus in the serum is not lowered.

With children suffering from rickets FABER (42) finds a small quantity of phosphorus and, in most cases, a decreased quantity of calcium without, however, any relationship seeming to exist between them. He maintains that blood changes form the primary symptoms of rickets. Normally, the relationship between calcium and phosphorus in the blood is practically the relationship of the two substances in $\text{Ca}_3(\text{PO}_4)_2$ (HOWLAND and KRAMER) (44).

According to HOLT (45) it is therefore obvious that a lack of one of the two substances in the blood will delay the process of calcination. Therefore, if the quantity of the two substances in the serum could be maintained by an extra supply of both given in the diet, a partial counteraction of the appearance of rachitic symptoms should be expected. FABER (42) and others, however, have found that the addition of phosphorus causes an increase in the quantity of phosphorus in the serum and a decrease of calcium, while the addition of calcium causes an increase in the quantity of calcium in the serum, and a decrease in phosphorus. The effect of calcium salt, even intravenously administered as will be stated later, (see table page 76 in register) and as SALVESEN (46) has shown, is exceptionally rapid and transient in its effect upon the calcium in the serum. FABER says the same is the case with the addition of primary or secondary sodium phosphate and its effect upon the quantity of inorganic phosphorus in the serum. Finally, FABER finds that the supply of secondary or tertiary calcium phosphate causes an increase of both low

calcium and low phosphorus in the serum, but if medication ceases, the original low values return immediately. The fact, therefore, that it is the ability to retain calcium and phosphorus, and not the ability to resorb, which suffers most during rickets, seems obvious.

3. Plan of own Investigations.

The purpose of these experiments was to examine calcium and phosphorus metabolism during the development, the existence, and the improvement of experimental rickets.

Puppies were employed as test animals, and as a standard rickets-producing diet that used by MELLANBY (47) was given, with a slight modification, viz.,

Skimmed Milk powder	20 %
Oatmeal	80 %

with the necessary addition of salt and vitamins (see later).

The plan was to examine concurrently the mineral metabolism of normal and sick animals, and also during the process of the healing of the disease by cod-liver oil. Further, the intention was to examine the mineral metabolism during the lack of, and the addition of, Vitamin C in the case of both normal and rachitic dogs.

Finally, to examine metabolism after having added to the standard diet either a calcium salt or a phosphoric salt, or both, thereupon after having replaced oatmeal in the diet with another kind of flour, to compare the influence of the various kinds of flour on the mineral metabolism, and their ability to develop experimental rickets.

A. Methods of Examination.

a) Animals utilised.

Puppies were utilised throughout.

Investigations were undertaken in 5 separate series, 21 puppies in all, designated in the Register of Experiments as Nos. I—XXI, being employed.

1st. series	consisted of 5 animals	Nos. I—V
2nd. »	» » 5 »	» VI—X
3rd. »	» » 4 »	» XI—XIV
4th »	» » 4 »	» XV—XVIII
5th »	» » 3 »	» XIX—XXI.

The animals of each separate series were of the same litter. Each series was, in most respects, the same in weight and development and, nourishment excepted, they lived under the same conditions, and thus could be mutually compared.

In the case of the first group of animals (mongrels) the tests began when they were 7 weeks old. They had then been suckled for 5 weeks and had afterwards lived on maize-oatmeal porridge with skimmed and unskimmed milk and bread for 2 weeks.

The puppies of the *2nd. group* were of pure grey elk-hound breed. They were taken for the tests when 8 weeks old and had then been suckled for 5 $\frac{1}{2}$ weeks and for 2 $\frac{1}{2}$ weeks had received the same diet as the 1st. group. About the middle of the experimental period these puppies were found to have round-worm, which, severely affecting the rickety dogs in particular, were cleared out with the help of 2 gm. semen arcae and 1 tablespoonful of castor oil administered by means of a stomach-tube.

3rd. group was of the same cross-breed as the 1st. group. The puppies were taken for experiment when 9 weeks old, after having been suckled for 5 weeks, and having had for 4 weeks the same diet as the 1st. group.

4th group, of which the mother was a pure, grey, elk-hound, and the father a German sheep dog, were taken for experiment when 5 weeks old, were suckled for 4 weeks and received a diet for 1 week similar to the groups above-mentioned.

5th group was of the same breed as 1st. and 3rd. groups. They were taken for experiment when 6 weeks old, after having been suckled for 5 weeks and on ordinary diet for 1 week.

b) Methods employed during periods of metabolism.

Investigations regarding metabolism were conducted in the manner usually employed, the animals being kept in special kennels for periods of 3 days at a time. The animals were weighed at the beginning and at the end of the period, the food consumed during the period also being weighed.

Urine was collected in the usual manner and kept under toluol. Urine from the 3 day period was mixed and measured, and from this total amount, samples were taken for analysis.

In the faeces the beginning and end of each period was marked by charcoal administered by stomach-tube.

Faeces were removed from the kennel as speedily as possible and kept in glass and under cover. The total amount for the 3 day period was stirred up well together, a process which as a rule, gave to the faeces the consistency of porridge, samples thereupon being taken for analysis.

Blood tests were made from veins in the hind legs of the animals.

c) Nourishment.

The diet employed to produce rickets was, in most respects, that employed by MELLANBY (47) and consisted of oatmeal and milk powder of skimmed milk.

At first, the finely-ground oatmeal was heated at 120° for one hour. This was done so that the animals would eat better but when later it was seen that they ate raw oatmeal just as well as that which had been heated, the process was discontinued. This has had no influence on the progress of the experiments.

There was added to the meal so much skimmed milk powder that the diet came to consist of:

Skimmed milk powder	20 %
Oatmeal	80 %

both considered as dry substances.

Analyses of *oatmeal* used for the experiments showed a content of:

Ca	from 0.059 to 0.066 gm. in 100 gm. dry substance
P	» 0.165 » 0.173 » » 100 » » »
Mg	» 0.107 » 0.139 » » 110 » » »

with average value of:

Ca	0.061 gm. in 100 gm. dry substance
P	0.171 » » 100 » » »
Mg	0.127 » » 100 » » »

with relationship Ca:P:Mg as 1:2.79:2.08.

Analyses of the *skimmed milk powder* showed:

Ca	from 1.042 to 1.049 gm. in 100 gm. dry substance
P	» 0.948 » 0.945 » » 100 » » »
Mg	» 0.107 » 0.111 » » 100 » » »

with average value of:

Ca	1.043	gm.	in	100	gm.	dry	substance
P	0.944	»	»	100	»	»	»
Mg	0.109	»	»	100	»	»	»

and relationship Ca:P:Mg as 1:0.905:0.105.

The calcium, phosphorus, and nitrogen content in the prepared diet mixture, varied to some degree in the various compounds, but within narrow limits.

For the 1st. litter, the average in 100 gm. of dry substance was:

Ca	0.242	gm.
P	0.352	»
N	2.28	»

Relationship between calcium and phosphorus as 1:1.414.

For the 2nd. litter, the average in 100 gm. of dry substance was:

Ca	0.277	gm.
P	0.313	»
N	1.94	»

Relationship between calcium and phosphorus was then as 1:1.129.

For the 3rd. and 4th litters no nitrogen analyses were taken. The average in 100 gm. of dry substance was:

Ca	0.321	gm.
P	0.310	»
Mg	0.126	»

consequently the relationship between calcium, phosphorus and magnesium was as 1:0.966:0.393.

The oatmeal-milk powder diet was weighed in a dry condition, stirred and mixed thoroughly with distilled water to the consistency of porridge and eaten by the animals in this form.

10 c.c. cod-liver oil¹ per diem was added to this diet when given to the control animals and to the diet of the animals used for developing rickets, 10 c.c. hardened coconut oil, together

¹ In the first series "Gadus" cod-liver oil was used, for the others, PETER MÖLLER'S cod-liver oil, without influencing the experiments at all.

with 5 gm. yeast extract or marmite, and, finally 1.5 gm. NaCl per diem, being added. All dogs, with the exception of Nos. I—V and No. X received, moreover, 5 c.c. lemon juice per diem. In order to assure that the animals consumed these various substances, they were added to a smaller daily portion.

The same was the case with the salts (calcium lactate, secondary natrium phosphate and, for No. XIII, a salt mixture) which, later during the experiments were given to some of the animals. Finally, all the animals were given as much distilled water as they wanted.

The animals could always eat as much of the diet as they desired but the quantity of food was weighed in a dry condition before being prepared.

The first litter of puppies Nos. III—V, with No. III as control animal, was put on the above-mentioned oatmeal-milk powder diet without lemon juice and were examined with particular regard being paid to the calcium and phosphorus metabolism. It was accordingly the intention when the disease was florid, to attempt a cure where one sick animal was concerned, by merely replacing the 10 c.c. hardened coconut oil per diem in the diet by 10 c.c. cod-liver oil per diem, thus, in later investigations regarding metabolism, being able to form an idea of the influence of cod-liver oil on calcium and phosphorus retention.

It was also intended in later examinations (2nd. Series) to investigate the influence of an addition of lemon juice alone or lemon juice and a calcium salt or phosphoric salt on the calcium and phosphorus metabolism respectively and on the rachitic symptoms. These last examinations, moreover, were also to be repeated on the animals of the 3rd. Series.

Further, in the 4th Series some changes were made in the composition of the diet itself, something which was also partially done towards the end of the metabolism investigations of the 3rd. group of which mention is made later. In the 4th group, one animal (No. XV) was given the «standard diet» referred to, the next (No. XVI) wheat flour instead of oatmeal, and the next (No. XVII) oatmeal only and not milk powder. This was done in order to examine still better the changes in metabolism.

Finally, in the 5th group, on the same diet, with a view to seeing the influence of large doses of calcium and phosphorus respectively, calcium lactate was added to the diet of one animal and sodium phosphate to the diet of another.

All the animals in the 4th and 5th series were given lemon juice.

d) **Methods of examination of calcium, phosphorus and magnesium quantities.**

a) *Determination of calcium in blood serum.*

TISDALL's (48) method was here employed.

b) *Determination of inorganic phosphorus in blood serum.*

The colorimetric method described by BRIGGS (49) with the modification of TOVERUD (50) was here employed.

c) *Determination of calcium, phosphorus and magnesium in urine.*

100 c.c. of urine was taken from the quantity collected during the three day period and calcination was undertaken by acid.

The determination of calcium was conducted on the basis of McCRUDDEN's (51) method, as modified by SHOHL (52), SIMPSON and TOVERUD (50).

The determination of phosphorus was carried out according to BRIGG's method. The standard solution was 0.1 or 0.2 mgm. phosphorus in 1 c.c. of solution. A 5 c.c. ammonia-molybdate solution was utilised with the addition of the 3 c.c. of 2% hydroquinon solution before the sodium-sulphite solution, as a better colour was secured in this manner. The colour was developed in a 100 c.c. measuring retort.

The determination of magnesium was executed according to BRIGG's method (49).

d) *The determination of calcium, phosphorus and magnesium in faeces.*

25 gm. faeces were weighed and ashed. The ash was dissolved in 10 c.c. N/1 HCl and diluted to 200 c.c. Of this 50 c.c. were taken for determining the calcium and magnesium as well as 5 c.c. for determining the phosphorus, in accordance with the same methods described for urine.

e) *The determination of N in urine and faeces was executed according to KJELDAHL's method.*



f) Analyses of bones.

As soon as possible after the death of the animal the bones were cleaned, prepared, weighed and then put in 96 % alcohol. After six weeks they were divided into smaller pieces and extracted with ether in SOXLETH's apparatus for 2×3 hours, each bone thereupon being dried in an electric drying cupboard at 100°—105°. They were then pulverised as fine as possible and again dried at 100°—105° to a constant weight.

Of the bone-powder about 1 gm. of the substance was weighed and ashed (to determine the amount of ash), being again dissolved in 10 c.c. N/1 HCl, and thinned further to 200 c.c. in a measuring retort. Calcium, phosphorus and magnesium tests were thereupon made in this solution in accordance with the methods previously described.

Double analyses were made everywhere with the exception of the blood.

g) Clinical symptoms of rickets in dogs.

It will be stated at the outset how the diagnosis of each particular dog is determined.

As is the case with children, rickets in dogs betrays itself by revealing its most pronounced symptoms, namely those of the bone system. One is struck first and foremost by the swelling of the rib-cartilage junction («rosary»), and by the swelling of the epiphyses of the long-shafted bones. In more marked cases curvature of the legs and some difficulty when walking will follow.

The diagnosis in these experiments has been based upon the swelling of the distal ulna and radius epiphyses and «rosary» and in each case the diagnosis is supported by an X-ray photograph. Autopsy or microscopical pictures of the bones have in no case disproved the diagnosis; on the contrary, they have supported it.

As will be observed from the register of experiments, the time of the appearance of rachitic symptoms varies somewhat. The main reason for this is to be found in the varying ages of the puppies when taken for experiment; it is, of course, a well-known fact that the older the subject, and the longer it has been on normal diet, — in the present cases, moreover, with the addition of cod liver oil, — the better it is able to resist the effect of a rickets-producing diet.

1st. Series:	Taken when 7 weeks old; clinical rachitic symptoms after 2—3 weeks.
2nd. " " " 8 " " " " " " " 5 "	
3rd. " " " 9 " " " " " " " 4—5 "	
4th " " " 5 " " " " " " " 3—4 "	
5th " " " 6 " " " " " " " 2—3 "	

Of the 21 dogs used for these experiments, four receiving cod-liver oil were control animals and with them no pathological bone changes appeared. Of the other 17, one, No. XIV, died from gastro-enteritis as early as six weeks after being taken, without any clinical bone symptoms being apparent. The remaining 16 (see Register of Experiments) all showed more or less pronounced rachitic bone symptoms, both clinical and radiographical.

B. Series of Experiments.

The investigations regarding metabolism have been made in five series. The results obtained from these various groups will be discussed singly, so that, later, a general review can be taken of the results as a whole. A table is given here of the various animals in order to assist the more detailed description of the tests given later. The complete register of experiments is given at the end.

1st. Series.

No.	I.	Oatmeal-milk powder + 10 c.c.	Cod-liver oil.	Control for No. II.
				No metabolism.
II.	"	"	+ 10 "	Coconut oil. Rickets.
III.	"	"	+ 10 "	Cod-liver oil. Control for Nos. IV and V.
IV.	"	"	+ 10 "	Coconut oil. Rickets. Later treated with cod-liver oil.
V.	"	"	+ 10 "	Coconut oil. Rickets.
				No dog was given lemon juice.

2nd. Series.

No.	VI.	Oatmeal-milk powder + 10 c.c.	Cod-liver oil.	Control for Nos. VII to X.
VII.	"	"	+ 10 "	Coconut oil. Rickets.
VIII.	"	"	+ 10 "	" " + 2 gm. Na_2HPO_4 .
				Rickets.
IX.	"	"	+ 10 "	Coconut oil. + 2 gm. Calcium Lactate. Died early.
X.	"	"	+ 10 "	Coconut oil. Not lemon juice.
				Discharged from experiment.

3rd. Series.

No.	XI.	Oatmeal-milk powder + 10 c.c. Coconut oil.	Control for Nos. XII to XIV. Rickets.
	XII.	" " " + 10 " Coconut oil. + 2 gm. Calcium lactate.	Rickets.
	XIII.	" " " + 10 " Coconut oil. + 5 gm. Salt mixture.	Rickets.
	XIV.	Wheat-flour milk " + 10 " Coconut oil.	Killed early owing to acute gastro-enteritis.

4th Series.

No.	XV.	Oatmeal-milk powder + 10 c.c. Coconut oil.	Rickets.
	XVI.	Wheat-flour milk " + 10 " " " "	" " " "
	XVII.	Oatmeal " + 10 " " " "	" " " "
	XVIII.	Ordinary dog's diet + 10 " Cod-liver oil.	Killed as a normal dog for Control for Nos. XV to XVII.

5th Series.

No.	XIX.	Oatmeal-meat + 10 c.c. Coconut oil.	Rickets.
	XX.	" " " + 10 " " " + 2 gm. Calcium lactate.	Rickets.
	XXI.	" " " + 10 " Coconut oil. + 3 gm. $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$.	Rickets.

All dogs, Nos. VI to XXI, excepting No. X, were given lemon juice.

No. IX which received in its diet a super-addition of 2 gm. calcium lactate per diem but which died during the experimental period, was replaced by No. XII in the next series. The same is the case with No. XIV which was given wheat-flour instead of oatmeal in its diet. It died early from acute gastro-enteritis (? distemper) and was replaced by No. XVI in the next series.

1st. Series of Experiments.

Calcium and phosphorus metabolism of a normal dog, a rickety dog and a rickety dog treated with cod-liver oil, on a diet lacking Vitamins C and D.

Of the first litter of puppies, three male dogs (III, IV & V) were chosen for investigation regarding calcium and phosphorus metabolism. Of these, No. III received cod-liver oil as a control animal for the two others which were given

coconut oil in order to produce rickets. Nos. I and II were not used for metabolism examination as, when their rickets became pronounced, they were killed for microscopical research. (59).

When 7 weeks old the puppies were put on a rickets-producing diet without lemon juice. To begin with all ate very well, about 200 gm. dry diet per diem, which, according to MELLANBY (47), is a factor of importance, as the more the animals eat the more rapid and pronounced does rickets become. As early as 3 weeks afterwards the first symptoms of rickets appeared. In the course of the following 17 weeks the rachitic bone ailments became greater and greater, weight remained constant (see fig. 66), appetite fell off, and walking became more and more difficult and awkward.

Repeated X-ray photographs of the distal radius and ulna epiphyses showed a condition exactly resembling human rickets, of lack of lime deposition, a thickening of the epiphyses and increased epiphyseal cartilage, as well as serration of the surfaces of the joints.

After 9 weeks one of these experimental animals (IV) was given 10 c.c. cod-liver oil per diem instead of coconut oil. This was done in order to observe the influence of cod-liver oil on calcium and phosphorus metabolism, as, on the one hand there was an animal quite normal from the commencement, and, on the other, a rickety animal whose condition continued to grow worse. The condition of the rickety animal in receipt of treatment improved rapidly and both the «rosary» and the epiphyseal swelling disappeared (see figs. 5—8). The developed curvature of the legs remained the same, however. Like the other two animals, it was killed when 24 weeks old, but it must be said that, from a clinical point of view, it was cured before being killed.

Control animal No. III, which from the commencement had been given 10 c.c. cod-liver oil per diem, kept well and active the whole time and presented neither clinical nor radiographical symptoms of rickets (see figs. 1 and 2).

No. V which received the rickets-producing diet throughout,

was severely affected by the disease, particularly during the latter part of the experiment. The dog had a poor appetite, kept very quietly in its kennel, had marked clinical and radiographical bone changes, (see figs. 11 and 12) the fore-legs in particular being bowed, and, towards the end, could hardly walk.

The results of investigations into the metabolism of these 3 dogs are collected in the accompanying table No. 1 and included therein, are the conclusions arrived at regarding calcium and inorganic phosphorus in the blood serum. In this, as well as in the other tables relating to calcium, phosphorus or magnesium, the balance values are expressed in grams for the complete 3 day periods, not worked out per diem. Further, + signifies that the intake through nourishment has been greater than the excretion through faeces and urine: positive balance; and — signifies that the animal has excreted more than received: negative balance.

A study of the table shows that where the rickety animal is concerned, there is a marked negative phosphorus balance throughout the whole period of experiment (17 weeks) so that phosphorus is steadily lost; moreover *an obvious positive, becomes an obvious negative sinking calcium balance*. At the same time *the amount of inorganic phosphorus in the blood serum sinks* from the normal 8.00 to below half, 4.00 mgm. per 100 c.c. serum and the amount of calcium sinks from the normal 10.6 to 6.76 mgm. in 100 cc. serum.

PINCUS, PETERSON and KRAMER (53) find varying normal calcium and phosphorus values in the blood serum of dogs, viz., 11.8—9.2 mgm. Ca, and 7.4—3.3 mgm. P in 100 c.c. serum. These values are for grown dogs; therefore, on the analogy of values of human adults and children, the values of the inorganic phosphorus in the serum where puppies are concerned, must be on a higher level. The values in cases of the normal puppies in these experiments, vary for inorganic P, from 8.00—8.88. According to HOWLAND and KRAMER'S *theory* the product of the inorganic P and C in mgm. in the serum of normal children is 40 or larger, but when rickets is either present or being cured the product is under 40.

Table 1.

Showing calcium and phosphorus balances as well as Ca and P in blood serum in the case of a control dog (III), a rickety dog treated (IV) and of a dog with rickets. No lemon juice given.

Date	Dog No. III. Control. Oatmeal. Skimmed milk powder + 10 cc. Cod-liver oil.				Dog No. IV. Treated Rickets. Oatmeal. Skimmed milk powder + 10 cc. coconut oil.				Dog No. V. Rickets. Oatmeal. Skimmed milk powder + 10 cc. coconut oil.			
	Mgm. in 100 cc. serum	Ca gm.	P gm.	balance	Mgm. in 100 cc. serum	Ca gm.	P gm.	balance	Mgm. in 100 cc. serum	Ca gm.	P gm.	balance
1925-6												
12-15/11	10.55	8.00			10.65		8.42		10.60	8.00		
19-21/11	10.55	8.32			10.37		7.65		10.55	8.32		
26-28/11	10.60	8.28		+0.01	10.15		7.20	+0.53	10.35	7.92		-0.20
1-3/12	10.71	8.72		+1.37	9.26		6.80	+0.80	10.74	7.08		+0.45
5-7/12	10.50	8.52		+0.49	9.12		6.48	+1.05	10.00	6.48		+0.96
10-12/12	10.68	8.74		+1.06	8.92		6.48	+0.02	10.23	6.72		-0.28
16-18/12	10.60	8.38		+2.12	7.17		6.80	+1.08	7.54	6.24		-1.16
20-23/12	10.20	8.78		+2.05	7.24		7.88	+0.01	9.19	6.68		-1.23
28-31/12	10.76	8.81		+1.71	6.98		7.42	+0.55	7.72	5.64		-0.70
4-7/1	10.42	8.65		+1.58	7.50		6.15	+0.43	8.42	5.34		-0.53
10-13/1	10.80	8.88		+2.21	6.58		5.68	+0.42	6.98	4.68		-1.37
16-19/1	10.05	8.68		+2.97	9.14		8.40	+1.63	9.14	6.04		-0.00
22-25/1	10.50	8.32		+2.97	9.14		8.08	+1.79	7.76	4.76		-0.45
28-31/1	10.46	8.64		+3.21	10.46		8.60	+1.52	7.28	5.48		-0.99
3-6/2	10.48	8.88		+3.56	10.81		8.16	+1.81	6.98	4.84		-0.93
9-12/2	10.85	8.60		+3.66	10.76		8.76	+2.50	7.42	4.80		-0.74
15-18/2	10.72	8.60		+4.01	10.48		8.00	+1.93	6.98	4.60		-0.84
21-24/2	10.68	8.40		+2.28	10.42		8.68	+3.87	6.98	4.20		-0.88
27-2/3	10.64	8.60		+5.18	10.48		8.60	+3.59	6.80	4.12		-0.25
5-8/3	10.56	8.40		+3.62	10.48		8.32	+3.01	6.76	4.00		-0.30
				+3.62				+2.74				-1.18

¹ 10 cc. cod-liver oil in 24 hours.

As the normal quantity of inorganic P is more than 8 mgm. and of Ca more than 10 mgm. in 100 c.c. serum in puppies, the product of Ca-conc. \times P-conc. in the serum of normal puppies is 80 or larger. Rachitic puppies may therefore have a Ca-conc. \times P-conc. product in the serum of under 80 but it does not need to be less than 40. It is easily apparent from Table 1 that the product of Ca-conc. and P-conc. in the serum is less than 80 for the rickety animal, while being 80 for the control animal (III).

Several investigators, SHOHL and BENNET (54) and others, have found in rickets a lowering of calcium and of inorganic phosphorus in the serum during rickets, while McCOLLUM and co-workers (55) maintain that there are two kinds of rickets, viz., the one with normal calcium and a low inorganic amount of phosphorus, the other with normal inorganic phosphorus and a low amount of calcium in the blood. According to what has been found in the present investigations, another kind of rickets must also be included, viz., rickets where the amount of both calcium and inorganic phosphorus in the blood is low, or the condition found is due to the lack of both Vitamins C and D, thus not rickets proper but a combination of rickets and scurvy or a scurvy-like condition.

In the case of No. IV an obvious negative phosphorus balance is seen during the first 9 weeks of the experiment and, further, a sinking calcium balance, exactly as in the case of No. V. As mentioned, after 9 weeks No. IV was treated for its disease with cod-liver oil which immediately gave rise to a marked positive phosphorus balance as well as to a calcium balance, increasing in strength — an effect of cod-liver oil which has long been recognised (SCHABAD 1909, BIERK 1909, MEYER 1913 and ORGLER 1912). With No. IV the amount of inorganic phosphorus in the serum sank from 8.12 to 5.08 mgm. in 100 c.c. serum, parallel with the negative phosphorus balance. Thus, when the animal was given cod-liver oil, the amount of phosphorus, so soon as 4 days afterwards, rose to the normal value of 8.00 mgm. in 100 c.c. serum (see Table 2) and remained there until the end of the experiment, whereas the

amount of calcium in the serum sank in 9 weeks from the normal value 10.65 to 6.58 mgm. in 100 c.c. serum. After 4 days on doses of cod-liver oil, however, it had risen to 9.14 and after 16 days to the normal value, 10.40 mgm. in 100 c.c. serum. Accordingly, in this one experiment it is seen that (Table 2) *when dosing with cod-liver oil, the amount of calcium in the serum takes longer to reach a normal value than does the amount of inorganic phosphorus.*

Table 2.

Dog No. IV. Increase of the amount of calcium and phosphorus in the serum during the days immediately following the commencement of dosing with cod-liver oil.

Date	Number of days after dosing with cod-liver oil had commenced	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum
10/1/26	Just prior to 1st. dose	6.58	5.08
11/1	1	7.49	6.48
12/1	2	8.40	6.83
13/1	3	8.81	7.00
14/1	4	9.14	8.00
18/1	8	9.14	8.40
22/1	12	9.14	8.08
26/1	16	10.40	8.48

Finally, on looking at the metabolism of the control animal, No. III, a constant positive phosphorus balance as well as a marked constant positive calcium balance, is seen during the whole experiment. The amount of inorganic phosphorus in the serum was maintained throughout, between 8.00 and 8.88 in 100 c.c., and during the same time, the amount of calcium only varied from 10.05 to 10.85 mgm. in 100 c.c. serum. If the positive phosphorus balance were to be determined according to the value which LIPSCHÜTZ (38) assigns to his normal dogs as the normal phosphorus discharge per diem, viz., 0.144 gm. P per kg. weight of body, very high figures would soon be reached, and, for the control animal, the apparently good P-retention would soon prove to be poor. (HEUB-

NER gives a similar value for growing dogs, viz., 0.14 gm. P per kg. weight of body per diem.) Thus, during the 4th period of metabolism the animal weighed 5.5 kg., and should therefore retain $0.144 \times 5.5 = 0.792$ gm. P per diem, or for the whole period of metabolism (3 days), $0.792 \times 3 = 2.376$ gm. P. The retention, however, is only 1.368 gm. P, a deficit of 1.008 gm. P, and only 57.52% is retained of the amount which should be necessary. The same would be the case for the last period when the weight was 17.6 kg., $0.144 \times 17.6 \times 3 = 7.602$ gm. P, while the retention was 3.619 gm. P, a deficit of 3.983 gm. P in 3 days and only 47.61% of necessary P-retention. If, therefore, the value for normal P-retention of a growing dog as given by LIPSCHÜTZ and HEUBNER, is correct, the reason why the control animal No. III remained normal, clinically, radiographically and microscopically, must be looked for in the cod-liver oil, which, as PARK and co-workers (56) maintain, does not act merely as a regulator of calcium and phosphorus metabolism but also permits of the organism operating with greatly increased economy. It could, however, be thought that the animal was not able to retain more phosphorus, because the calcium retention was so great. According to ORR and co-workers (57) an excessive amount of calcium in the diet, will, namely, tend to decrease phosphorus retention, but it can hardly be thought that in the diet mentioned (see page 18) there is an excessive amount of calcium for the diet of a dog.

SCHABAD (33) finds that increased excretion of calcium in faeces leads to retention of phosphorus, and the reverse. If, therefore, in the case of dog No. III there were a small excretion of calcium through the faeces, a probable explanation of this low P-retention compared with the figures of HEUBNER and LIPSCHÜTZ, is found.

During the 4th period of metabolism of dog No. III there were excreted through the faeces 1.11 gm. Ca and 1.67 gm. P, while the total intake was 2.51 gm. Ca and 3.75 gm. P.

The values of the last periods of metabolism were: 1.68 gm. Ca and 4.26 gm. P excreted through faeces, total intake: 5.31 gm. Ca and 8.03 gm. P.

It is apparent, therefore, that in the 4th period of metabolism the Ca retention is 52.8 % of the intake and P retention 36.4 %, a relationship between Ca retention and P retention as 1:0.69 and for the last period of metabolism the Ca retention is 68.0 % of the intake and the P retention is 45.0 %, a relationship between Ca and P retention as 1:0.66. It is observed that the retention of both has increased while the relationship between them has not been greatly disturbed.

If the P retention in the 4th period had been 0.144 gm. P per kg. of the weight of the body, the animal must have retained 63.3 % of the intake, and in the final period the retention should have been 94.6 %.

If, however, one works out roughly how much phosphorus No. III would retain from the first day of life until the last day of the period of experiment, the animal, 168 days old, with a weight of 17.6 kg. would have retained altogether 190.9 gm. P. Thus, in 54 days of metabolism (see table) the animal has retained 27.91 gm. P. If this is calculated for the 168 days concerned, it will be seen that it has retained approximately 86.35 gm. P. Therefore, merely in the short period of 168 days the animal retained 104 gm. P too little.

If the phosphorus retention had really been poor, this fact must have found expression, if not clinically, then microscopically or chemically. Microscopically (SKAAR and HÄUPL (59)) the bones, in any case were normal. If one compares the results of the bone analyses with those of No. XVIII (see table) the sole animal which throughout received the ordinary diet of a dog, and, accordingly to be considered normal, it will be seen that the P-content in the bones varies exceptionally little for the two animals concerned, in fresh weight, dry weight and in bone ash.

MORGULIS (58) has found the following values in the femur of a grown dog (bull dog): 25.23 % calcium and 11.49 % phosphorus in dry weight and 37.64 % calcium, as well as 17.47 % phosphorus in the ash. The values vary exceptionally little from those found in animal No. III.

Table 3.
Showing results of bone analyses of Control puppy (III), rickety puppy treated (IV) and a rickety puppy (V).

Puppy No.	Bone	Water + Fat.	% Ash		% Ca in			% P in		
			Fresh w.	Dry w.	Fresh.	Dry.	Ash.	Fresh.	Dry.	Ash.
III. (Control.)	Femur	61.16	21.86	56.39	8.21	21.14	37.57	4.63	10.39	18.45
	Femur-shaft . .	58.65	25.33	61.30	9.24	22.37	36.50	4.95	11.98	19.54
IV. (Treated Rickets.)	Femur	69.50	16.17	52.23	5.82	19.14	35.96	2.63	8.64	16.24
	Femur-shaft . .	65.30	20.55	59.21	7.50	21.61	36.61	3.80	10.94	18.48
V. (Rickets.)	Femur	81.17	7.10	37.73	2.32	12.81	32.62	1.37	7.30	19.34
	Femur-shaft . .	—	—	45.94	—	15.95	34.72	—	8.73	19.00

Altogether it may certainly be said that everything points to the fact that the phosphorus retention of No. III during the period of experiment, has been sufficient to enable the animal to be considered absolutely normal; the normal P retention for growing dogs (0.144 gm. P per kg. weight of body per diem), as fixed by LIRSCHÜTZ and HEUBNER must accordingly be considered too high.

All three animals were killed 17 weeks after the experiments began, i.e., when 24 weeks old. The results of the various bone analyses will be found in the tables and there will, accordingly, merely be mentioned here as examples the differences which can be traced in the femur and femur shafts of the 3 animals, the analyses being collected in Table No. 3.

Regarding the fresh weight, a very considerable difference between the amount of calcium and the amount of phosphorus will be observed in the case of No. V, when compared with No. III, the control animal which was given cod-liver oil. The calcium and phosphorus content of the fresh bone of No. V lies 72 % and 66 % respectively below that of the control animal.

The fact that there was not found in the bones of No. IV, the animal which, during the second half of the period of experiment, was given cod-liver oil to cure the rickets produced, a percentage content of calcium and phosphorus corresponding to that found in the bones of the control animal, must show that the *deposition of calcium and phosphorus in the bones is slower than the clinical cure*. The animal when killed, was, namely, clinically cured of its disease. The epiphyseal swelling had disappeared, also the «rosary», but of course, some curvature of the legs, especially of the fore-legs, was noticeable. This can hardly be corrected, however, and, as the animal did not apparently improve during the course of the three last weeks, it was considered that the curvature would not diminish further. If, in order to obtain an explanation of the low Ca and P content of this animal, the macroscopical appearance of the bones of the animal (see figs. 9—10) is compared with that of the control animal, it will seem that both the rib-cartilage junction

and the tibia epiphyseal cartilage of the animal treated for rickets (IV) are not so even as in the normal animal (III) (Figs. 3 and 4). On the other hand, an exceptionally great improvement is seen in the case of No. IV as compared with No. V (figs. 13 and 14) where the rib-cartilage junction is very uneven, swollen and serrated, the tibia epiphyseal cartilage, moreover, being broader and also very uneven. The microscopical discoveries, the further details of which are of no concern here but which are described in another work (59), proved beyond doubt that in the case of No. V, a condition existed very similar to human rickets, and, in the case of No. III, no ailing changes resembling rickets could be found. Neither macroscopical nor microscopical changes in the bones showing evidence of scurvy were found in any of the animals experimented upon. In the case of No. IV, a partial late; calcification of the bones was found, as can also be seen during the healing of rickets in children.

Summary: From these three experimental animals, it is clear that, during the development and the florid stage of rickets in dogs on a diet lacking Vitamins C and D, an obvious negative phosphorus balance appears, and that the calcium balance is maintained positive for a considerable while before becoming negative. Further, cod-liver oil acts in such a manner that the negative phosphorus balance rapidly becomes positive and the weak positive calcium balance becomes strongly positive. When the amount of calcium and phosphorus in serum is below normal, phosphorus rises more rapidly to normal, when dosing with cod-liver oil, than calcium.

2nd. Series of Experiments.

Calcium and phosphorus metabolism of a normal dog, a rickety dog, and a rickety dog given a super-addition of calcium or phosphorus salt in the diet.

It was intended in this series to investigate how the addition of Vitamin C by lemon juice and the super-addition of a calcium or a phosphoric salt to the diet would influence the

respective metabolism during the rachitic condition. Comparisons had thus to be made in respect of both a normal control animal and an animal given the rickets-producing diet plus a super-addition of salt.

The therapeutical effect of both calcium and phosphorus has repeatedly been attempted but always with negative results. It was not to be expected, therefore, that these investigations would produce any preventative or curative influence as a result of the super-addition of salt.

In the case of the five dogs of this series, the rachitic condition, on the whole, develops slower. From the commencement these animals were already a week older (8 weeks), more grown, and they immediately ate more than the first puppies, viz., about 300—400 gm. dry diet per diem.

While the animals of group I were not given lemon juice, all subsequent animal groups received 5 c.c. lemon juice per diem in order to avoid any possible deficiency of *Vitamin C*, this being, however, an addition to the diet which should be superfluous as dogs are considered to be immune to scurvy, at all events, no such condition has ever been produced experimentally in the case of dogs.

No. VI as the control animal, was given cod-liver oil, and No. VII, coconut oil. With the exception, therefore, of the addition of lemon juice, these two should correspond to No. III and No. V respectively in the previous series of experiments.

If one looks at the periods of metabolism of these two dogs (Table 4) the difference is immediately seen even in the case of the cod-liver oil animal. The control animal No. VI shows from the commencement a much stronger positive calcium and phosphorus balance than No. III. There is also some difference in the relationship of No. VII and No. V, the calcium balance of the latter remaining, as mentioned, around nil, with the phosphorus balance being negative throughout, whereas for No. VII, the position is exactly reversed. This reversed relationship also finds expression in the amount of calcium and inorganic phosphorus in the blood serum of the two animals; with No. V, where the calcium balance

Table

Showing calcium and phosphorus balances, together with
Dogs Nos. VI—IX were given

Date	Dog No. VI. Oatmeal. Skimmed milk powder + 10 c.c. Cod-liver oil					Dog No. VII. Oatmeal. Skimmed milk powder + 10 c.c. coconut oil					Dog No. Oatmeal. milk powder coconut oil + 2	
	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca balance in gm.	P balance in gm.		Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca balance in gm.	P balance in gm.		Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum
1926												
8—11/5	10.16	8.41	+ 1.20	+ 1.83		10.65	8.48	+ 1.22	+ 1.50		10.65	8.41
14—17/5	10.16	8.69	+ 1.09	+ 2.00		10.68	8.16	+ 1.08	+ 1.70		10.89	8.15
20—23/5	10.39	8.75	+ 3.01	+ 2.78		9.90	8.24	+ 1.53	+ 1.53		10.16	7.01
26—29/5		8.69	+ 3.08	+ 2.78		10.22	7.73	+ 1.04	+ 1.70			8.12
1—4/6	10.65	8.69	+ 1.50	+ 2.34		9.74	7.76	+ 0.46	+ 1.44		9.71	8.20
7—10/6	10.16	8.28	+ 2.28	+ 2.88		7.78	7.76	+ 0.17	+ 1.15		8.78	7.64
13—16/6	10.16	8.05	+ 2.73	+ 3.40		7.78	7.64	+ 0.45	+ 1.13		7.30	6.96
19—22/6	10.16	8.00	+ 2.98	+ 2.89		7.78	6.54	+ 0.22	+ 0.95		7.30	6.68
25—28/6	10.38	8.12	+ 3.31	+ 2.97		6.82	6.82	— 0.13	+ 0.33		7.70	6.40
1—4/7	10.16	8.12	+ 3.13	+ 3.36		6.82	6.54	— 0.15	+ 0.73		7.22	6.40
7—10/7			+ 1.88	+ 2.91				+ 0.16	+ 0.86			
13—16/7	10.16	8.42	+ 0.66	+ 0.60		5.38	5.92	+ 0.00	+ 0.99		7.30	5.62
19—22/7	10.16	8.42				5.38	6.09				6.85	4.48
25—28/7	10.68	8.00	+ 2.11	+ 3.31		6.82					6.28	3.20
31/7—3/8			+ 1.77	+ 3.60				— 0.04	+ 0.77			
6—9/8	10.68	8.00	+ 3.49	+ 4.12		6.32	4.00	— 0.28	+ 0.62		6.82	3.67
12—15/8	10.68	8.20	+ 0.89	+ 4.25		6.32	3.72	¹ + 0.44	+ 0.42		6.32	3.90
18—21/8	10.19	8.20	+ 1.40	+ 2.96		5.87	4.32	+ 0.77	+ 0.10		5.87	3.81
24—27/8	10.68	8.60	+ 2.84	+ 3.63		5.87	4.49	— 0.79	+ 0.16		5.88	4.10
30/8—3/9	10.68	8.20	+ 2.60	+ 3.54		5.38	6.40	² — 0.00	— 0.06		5.78	3.64

¹ 5 gm. CaCO₃ in 24 hours.

² During this period no food was taken.

4.

Ca and P in serum of dogs of 2nd. Series of Experiments.

5 c.c. lemon juice per diem.

VIII. Skimmed + 10 cc. gm. Na_2HPO_4		Dog No IX. Oatmeal. Skimmed milk powder + 10 c.c. coconut oil + 2 gm. calcium lactate				Dog No. X. Oatmeal. Skimmed milk powder + 10 c.c. coconut oil			
Ca balance in gm.	P balance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca balance in gm.	P balance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca balance in gm.	P balance in gm.
+ 0.79	+ 1.24	10.36	8.48	+ 1.78	+ 1.01				
+ 1.57	+ 2.42	10.87	8.55	+ 2.07	+ 1.67				
+ 1.48	+ 2.86	10.87	8.14	+ 2.44	+ 1.58	10.72	8.18		
+ 2.10	+ 3.27		8.40	+ 2.27	+ 1.63	10.68	8.41	+ 1.50	+ 1.59
+ 1.43	+ 2.76	10.65	8.00	+ 2.35	+ 1.74	10.72	8.37	+ 1.39	+ 1.89
+ 1.10	+ 2.47	10.16	7.64	+ 1.35	+ 1.45	10.68	8.42	+ 1.25	+ 1.54
+ 0.60	+ 1.79	9.71	7.82	+ 1.62	+ 1.70	10.19	8.48	+ 2.11	+ 0.76
+ 0.61	+ 1.47	8.76	7.18	+ 1.46	+ 1.57	10.19	8.00	+ 2.09	+ 2.05
+ 0.34	+ 0.69	8.76		+ 1.18	+ 1.16	10.00	7.62	+ 1.61	+ 1.16
+ 0.58	+ 1.30	8.76	6.30	+ 0.90	+ 0.99	9.71	7.80	+ 2.27	+ 1.31
+ 0.32	+ 1.64			+ 1.01	+ 1.12			+ 1.26	+ 1.61
+ 0.82	+ 1.32	7.78	5.34	+ 0.65	+ 1.80	9.71	6.96	¹ + 1.11	+ 1.32
						9.71	6.58		
- 0.37	+ 0.55					10.68	6.74	² + 1.36	+ 1.41
+ 0.28	+ 1.70					10.19	7.62	² + 1.49	+ 2.19
+ 1.06	+ 1.55								
- 0.60	+ 0.33								
+ 0.22	+ 0.62								
- 0.16	+ 0.52								
- 0.16	+ 0.69								

¹ Lemon juice 5 c.c. per diem.² Cod-liver oil 10 c.c. per diem.

remains around nil, the Ca in the serum does not fall so rapidly, or so low (lowest 6.76 mgm. in 100 c.c. serum) whereas, the negative phosphorus balance sinks rapidly to so low as 50 % of the original value. On the other hand, for No. VII the amount of Ca in the serum falls more rapidly and lower (lowest 5.88 mgm. in 100 c.c. serum); the amount of the inorganic phosphorus in the serum corresponding to the phosphorus balance falling successively towards nil, also falls slower, and, only towards the end of the period of experiment, does it reach the depth No. V had already reached when about mid-way through the experimental period.

When the experimental period was well advanced, 5 gm. CaCO_3 per diem was administered to No. VII in order to observe the influence of such a large dose of calcium per os. on the metabolism. The calcium balance which had then been negative for a few periods went clearly up to positive during the first two periods after the dosing with calcium had commenced. At the same time the phosphorus balance continued to fall, but, as early as the third period after the calcium dosing had commenced, the balance was again negative, and as the animal then began to starve and it was feared that starvation would give rise to an improvement of the illness, the experiment was discontinued and the animal killed.

The variations found here in respect of the calcium and phosphorus balance of the two rickety animals, which, with the exception of the 5 c.c. lemon juice of the one, were otherwise on the same diet and lived under the same conditions, point decidedly to the fact that the lack of Vitamin C in connection with the lack of Vitamin D causes differences in the mineral metabolism.

CHANEY and BLUNT (60) have found that the addition of orange juice to the diet causes in the case of children a stronger retention of calcium and, further, a phosphorus retention three times as great as that without orange juice. Here it has also been found that the animal given lemon juice as an addition to the diet has a stronger calcium balance than the animal to which lemon juice was not given. One is there-

fore entitled to say that *the addition of lemon juice in cases of experimental rickets in dogs is a matter of importance where the calcium balance is concerned and it does not seem correct to presume that dogs are not liable to scurvy.*

It has long been known that the assimilation of both calcium and phosphorus in the organism at the same time is very disturbed by rickets as the retention of these elements in the organism is dependent on each other. *The experiments here discussed, however, should indicate that in the one case it is the calcium assimilation which is more frequently attacked, and in the other, it is that of phosphorus which is influenced most.*

The experiments with animals Nos. VIII and IX, of the same litter as Nos. VI and VII, were undertaken in order to ascertain what influence on the metabolism a calcium salt or a phosphoric salt would have, whether the development of the disease would be retarded or made worse. The animals were nourished in quite the same manner as No. VII, but in the case of No. VIII, 2 gm. Na_2HPO_4 (corresponding to 0.346 gm. P) per diem, and in the case of No. IX, 2 gm. calcium lactate (corresponding to 0.26 gm. Ca) per diem were added to the diet.

From a clinical point of view this super-addition of salt was reflected in the case of No. VIII («the phosphorus animal») (fig. 23) by the animal growing worse. Considerable epiphyseal swelling and «rosary» developed and, altogether, the animal grew much worse than No. VII (fig. 19).

No. IX (the «calcium» animal) also showed epiphyseal swelling and «rosary» but to a comparatively low degree only, and, altogether, it was clinically the least afflicted of all the sick animals.

At the commencement No. VIII evidenced a positive calcium balance which fell rapidly towards nil and, at last, when approaching the termination of the experiment, became negative. The calcium in the serum also fell rapidly and at the end of the period of experiment was about 45 % below normal value. The phosphorus balance of No. VIII remained fairly

high, fell a little, but only towards the end of the experiment, remaining, all the same on the positive side. When the phosphorus balance was still at its original level the amount of phosphorus in the serum fell so rapidly that towards the end of the period it became less than half the original amount.

If No. VIII is compared with No. VII, which did not receive a super-addition of salt in the diet, it will be noticed that, so far as the metabolism of the two animals is concerned, it is about parallel in the case of the calcium balance and that the phosphorus balance remains more strongly positive throughout with No. VIII which was given the sodium phosphate in addition.

From what ORR and his *co-workers* (57) have found, that excessive amounts of phosphorus in the diet give rise to an unfortunate influence on the calcium metabolism by the great loss of calcium excreted through the faeces, it would have been expected that the calcium balance of No. VIII would have proved poorer than was the case with No. VII. This, however, cannot be said to be the fact. KARELITZ and SHOHL (61) have also discovered that the calcium balance falls when phosphorus (Na_2HPO_4) is given extra in the diet, and that the phosphorus balance rises. SHOHL and BENNET (54) found in the case of rickety dogs a positive calcium balance, lower, however, than the normal, and a weak positive balance in the case of two animals and a negative phosphorus balance in one. Finally, in a diet rich in phosphorus and poor in calcium the deficiency of the phosphorus retention is more pronounced. So far as it goes, this agrees with what M. JONES (62) has found that, with rickety puppies, the increase of the one element, either calcium or phosphorus will, under certain circumstances, but not always, give rise to a larger retention of the one and a smaller retention of the other. Further, he found that the addition of Na_2HPO_4 to the diet of rickety animals, causes increased bone destruction of those affected to so large an extent that the bone ash of a dog 265 days old contained about half of that of newly born puppies. This is mentioned further below.

No. IX (the «calcium» animal) showed that, at first, the calcium balance was strongly positive and that it neither fell so rapidly nor so correspondingly as in the case of the «phosphorus» animal. The phosphorus balance of the «calcium» animal is less, but it maintains the same level throughout the whole period of experiment. Similarly, the amount of calcium in the serum remains longer within normal limits, falls slower and not so correspondingly low as in the case of the «phosphorus» animal. The amount of phosphorus in the serum which for long remains normal, falls, together with the last large fall of the amount of calcium, to about 70 % of its original value. Unfortunately, the «calcium» animal died suddenly about half-way through the period of experiment. Autopsy revealed some round worm in the intestines, otherwise nothing. The animal was found dead with marked opisthotonus. As will be seen from the next series of experiments, this animal was replaced by another which also received a super-addition of 2 gm. calcium lactate per diem, viz., No. XII, and the results of the two animals will accordingly be compared and discussed later. It will merely be mentioned here that, so far as the calcium retention is concerned, this seems to show what ORR and *co-workers* have found, that excessive amounts of calcium in the diet cause a rise in the total absorption and retention of calcium but tend to decrease the retention of phosphorus. On this point, however, there is no agreement as it cannot be said that the «calcium» animal had a worse phosphorus retention than the others — but rather a better.

By giving 3 gm. calcium lactate per diem to a normal adult, R. BERG (63) found that a marked discharge of calcium arose in the organism and if this should be the case the results of dosing the rickety puppy in this series of experiments should find expression in an increased amount of calcium in the bones of the animal. If, therefore, the results of the bone analyses in this group are examined, and consideration paid to the fact that No. IX died 6 weeks before the others and that it can therefore be thought that the quantities

of both calcium and phosphorus in the bones would accordingly have been a little higher, it must certainly be admitted that it is difficult to imagine that the normal values would have been approached.

Thus there are definite, reduced values for both calcium and phosphorus in the bones of No. IX but they are not nearly so low as in the case of the animal which did not receive the addition of salt (No. VII) or of the «phosphorus» animal (No. VIII) as they are for the control animal (No. VI).

The super-addition of Na_2HPO_4 to the diet which brought about, clinically, a worse condition, and which gave a stronger phosphorus balance than without the addition, gives the same result, so far as the bone content is concerned, as is given in the case of animal No. VII which did not receive the super-addition; compared, however, with the control animal, the quantities of both calcium and phosphorus are reduced. The calcium content of the «phosphorus» animal lies, partly, a little lower, and partly about the same level when compared with No. VII. Against this, when viewing the magnesium analyses which, unfortunately, are only included for the ulna and radius of the dogs, it will be observed that the phosphorus animal No. VIII has obviously decreased magnesium content in these bones when compared with No. VII. The question as to whether conclusions can be drawn from this will be returned to when the results of magnesium metabolism are discussed.

Histologically, however, No. VIII, showed no larger extension of the calcium-less bone zones than No. VII, while, in the case of No. IX, a less marked extension of the calcium-less bone zones was found.

As the results of the first metabolism periods in this series of experiments showed so much stronger a positive balance for all animals concerned when compared with the balances of the animals in the first series, and, as in the light of the discoveries of CHANEY and BLUNT (60) regarding orange juice, it could be thought that the origin of the stronger balances could be found in the addition of lemon juice to the diet,

Table 5.
Bone analyses of Control (VI), Rachitic (VII), «Phosphorus» (VIII) and «Calcium» (IX) dogs.

Puppy No.	Bone	% Water + Fat	% Ash in		% Ca in			% P in		
			fresh wgt.	dry wgt.	fresh wgt.	dry wgt.	ash	fresh wgt.	dry wgt.	ash
VI.	Femur	52.76	27.74	58.72	11.27	21.42	36.49	5.24	11.09	18.89
	Femur-shaft	45.76	33.93	62.52	13.15	24.23	34.58	6.62	12.19	19.50
VII.	Femur	70.00	13.80	46.02	5.43	18.08	39.31	2.66	8.85	19.24
	Femur-shaft	62.15	21.75	57.50	7.78	20.56	35.76	4.25	11.22	19.52
VIII.	Femur	71.06	13.26	45.84	4.90	16.93	36.95	2.56	8.85	19.32
	Femur-shaft	62.61	21.75	58.16	7.52	21.05	36.21	4.11	11.00	18.95
IX. ¹	Femur	66.71	16.28	48.90	7.20	18.63	38.11	3.04	9.14	18.68

¹ Died during experiment.

animal No. X was taken for experiment two weeks later than its fellows, viz., when 10 weeks old. No. X therefore, was given the same diet as No. VII, but *not lemon juice*. As is apparent from Table 4, both the calcium and phosphorus balances were strongly positive for the 11 weeks the animal was under experiment. After four weeks a faint epiphyseal swelling was apparent clinically, after 8 weeks faint epiphyseal swelling and «rosary» and, at the same time, slight rachitic bone changes, could be noticed radiographically (fig. 29). Chemically, the amount of inorganic phosphorus in the serum had undergone the greatest changes, as its amount after 8 weeks had decreased to 6.68 mgm. in 100 c.c. serum. The amount of calcium, however, did not sink lower than 9.71 mgm. in 100 c.c. serum.

In order to ascertain whether the addition of lemon juice to the diet would bring about still higher positive balances than already observed, the juice was added and the metabolism examined, without, however, any rise being detected in either the calcium or phosphorus balance.

The animal was thereupon given 10 c.c. cod-liver oil per diem during the two last periods of metabolism, and, as will be seen from the table, the addition of cod-liver oil did not give rise to an increase of the calcium balance, but only to an increase of the phosphorus balance during the final period.

When judging the results obtained from this animal, No. X, regard must be paid to its age at the time it was taken for the experiment. It was then 10 weeks old and had accordingly lived two weeks longer on ordinary diet with cod-liver oil added, a factor which it was known would render the animal less suitable for the test. Moreover, prior to undergoing experiment the animal had of course already benefited a considerable while from the abundance of the anti-rachitic vitamin in cod-liver oil and had probably gained a not inappreciable store which led to the rachitic symptoms developing, clinically as well as chemically, at an exceptionally slow rate.

With regard to the experiment on No. X, therefore, it is wrong to conclude otherwise than that, in the case of an

animal which has been somewhat longer on ordinary diet with an addition of cod-liver oil, the production of rachitic symptoms by giving a diet, otherwise strongly rickets-producing, proceeds much slower. *Where lemon juice is concerned, no other conclusion can be arrived at with certainty than that of saying that during this experiment no special calcium-retaining effect of importance appeared when compared with the other animals upon which experiments were undertaken.*

Summary:

The addition of lemon juice to a rickets-producing diet increases the calcium balance.

The changes in the mineral metabolism of rachitic dogs found in these experiments when Vitamin C is lacking, seem to indicate that dogs may also be afflicted by scurvy or scurvy-like conditions.

If a comparison is made of Nos. VIII and IX with No. VII, which received the same diet without any super-addition of salt, the following result of the experiment, is, on the whole, arrived at: *2 gm. Na_2HPO_4 added to a rickets-producing diet give, clinically, a more marked rickets; at the same time the phosphorus balance is stronger and the calcium balance about parallel with animals not in receipt of a super-addition of salt.* Where the chemical composition of the bones is concerned, the phosphorus content is the same, the amount of calcium, to some extent a little lower, but mostly the same, while the magnesium content shows a considerable fall.

2 gm. calcium lactate added to a rickets-producing diet, give, clinically, a less marked rickets, as well as a strong positive balance and a phosphorus balance which, compared to the non-addition of salt to the diet, is also strongly positive. The calcium and phosphorus contents of the bones are greater both with and without Na_2HPO_4 in the diet, but are not the same as in the case of the normal control animal.

3rd. Series of Experiments.

Calcium, phosphorus and magnesium metabolism in a rickety animal and of rickety animals which have been given a super-addition of either calcium salt or calcium phosphate.

As, as mentioned above, the animal of the previous group in receipt of a super-addition of calcium in the diet, died before the experiment was concluded, an attempt was made to put No. XII of this group in its place.

In order to study metabolism further by giving an extra large addition to the diet, No. XIII was given 5 gm. per diem of a salt mixture consisting of 840 parts $\text{Ca}_3(\text{PO}_4)_2$ and 95 parts CaCO_3 , corresponding to an amount of 1.98 gm. calcium and 0.55 gm. phosphorus per diem. According to AD. CARNOT (64) 875 parts calcium phosphate and 102 parts calcium carbonate are found in 1000 parts of ash from a human femur (corpus) while in the human femur (caput) there are 879 parts of calcium phosphate and 92 parts calcium carbonate. The salt mixture was composed, therefore, in this manner in order to approach the normal bone ash figure as closely as possible, and it was intended by giving such large doses of this mixture as 5 gm., per diem, to flush the organism as much as possible in the hope of obtaining the greatest possible retention in the organism.

As control animal for these two, animal No. XI was used. It received the same diet as No. V and No. VII, a diet on which rickets would easily be produced. The animals were put on the experimental diet when 9 weeks old and investigations continued for 32 weeks until they were 41 weeks old. The animals after having been suckled for 5 weeks were given an ordinary diet with the addition of cod-liver oil for 4 weeks, a factor which proved unfortunate for the progress of the experiment and which will be discussed later. Cod-liver oil was given here before the actual commencement of the experiment in order to ensure that the animals did not have incipient rickets from the very commencement and the lemon juice was given in such a manner that the rickets-producing diet was deficient in Vitamin D only. In order still further

to complete these investigations regarding metabolism, the determination of magnesium metabolism was also undertaken from the middle of this period of experiment. As, however, the development of rickets proceeded exceptionally slowly, both clinically and chemically (see Table 6), the experimental diet as from 26.11.27 was changed, the animals being then 29 weeks old and under experiment for 20 weeks, by the withdrawal of the milk powder so that oatmeal only was given with the various salt additions as before.

When the results of these metabolism investigations are viewed (Table 6), it will immediately be observed that all animals during the first 12 metabolism periods have large, obviously positive calcium and phosphorus balances, most marked in the case of No. XIII («calcium phosphate» animal). While this animal has a calcium balance which shows a tendency to fall (the phosphorus balance is about the same level) it is very difficult to determine whether this is a physiological fall due to the animal requiring a decreasing supply of calcium because the main period of growing has ceased, or whether it is a fall depicting incipient rickets. Against a «physiological» fall is the age of the animal — it was then not more than between 20 and 27 weeks old and a dog cannot be considered as fully grown before it is two years old. Further, if it were physiological the amount of calcium in the blood serum ought to be within normal limits, but during the period concerned it was 8.60 mgm. Ca in 100 cc. in the serum, a clear reduction, while the amount of inorganic phosphorus in the serum consequent upon the high level of the phosphorus balance during this period remains normal, 8.40—8.42 mgm. P in 100 cc. serum.

It will be seen that, during the continued experiment on the animal, the metabolism period of 13th—19th, when the animal was given oatmeal only to eat instead of the original oatmeal-milk powder diet, the calcium balance turns negative, and, at the same time, the amount of calcium in the serum falls so low as 6.08 mgm. in 100 cc. Further, there is a clear fall in the phosphorus balance which, although it maintains itself positive throughout, is weakened as a result of the re-

duction of the inorganic phosphorus in the serum to 3.88—4.21 mgm. in 100 cc. This, taken in conjunction, everything points to the falling calcium balance which is evident in No. XIII from the 7th to 11th period of metabolism, being due, not «physiologically» but to the incipient development of rickets.

If the tertiary calcium-phosphate given to the organism, is excreted as such through faeces as is maintained by R. BERG (63), ORR and co-workers (57), the only active super-addition of salt in the case of No. XIII would then be the CaCO_3 mixed with the tertiary calcium-phosphate and which per diem represents 0.194 gm. calcium. It is inconceivable, however, that this comparatively low amount, even less calcium extra per diem than with No. XII, should be able to exert such a beneficial influence on both the calcium and phosphorus balance, as, according to what was revealed in the case of No. VII which during the last four periods of metabolism received the addition of 5 gm. CaCO_3 equal to 2 gm. calcium per diem, this had merely a transitional effect on the poor calcium balance and none at all on the phosphorus balance.

It must therefore be considered reasonable that the large amount of calcium phosphate administered has in this case had a beneficial effect on both the calcium and phosphorus balance. In the first period of metabolism where the animal did not receive in the diet so much calcium as it retained viz., 2.75 gm. Ca, it must, when is added to this the calcium amount in the CaCO_3 addition per diem, have retained 0.72 gm. calcium of tertiary calcium-phosphate. According to the conditions under which the experiments were conducted, it must thus be said that here in the case of No. XIII calcium of tertiary calcium-phosphate has been resorbed, at any rate, during the first period of metabolism. With regard to the later periods of metabolism where the balances were not large enough to enable a direct calculation being made of how much calcium from tertiary calcium phosphate the animal must have retained, there is no refutation that this has not been the case.

Even though it must be considered certain that the administration of large quantities of $\text{Ca}_3(\text{PO}_4)_2$ in a rickets-producing

diet causes an increase of both calcium and phosphorus balances, they do not counteract completely the rickets-producing quality found in oatmeal as, clinically, radiographically and microscopically, rachitic bone symptoms, although weak, were obviously present.

With Nos. XI and XII there are found, as mentioned, positive balances during the first 12 periods of metabolism but, in the case of each animal there is a fall in the calcium and phosphorus balances just as there is a fall in the amount of both Ca and inorganic P in the serum. As in the case of No. XIII this must be taken as a sign of the development, even if slow, of rachitic symptoms. The supply of milk powder was also stopped from the 13th—19th metabolism period in the case of these two dogs, and, as with No. XIII, a speedy change in the balances resulted.

With No. XI, which was not given any super-addition of salt, the phosphorus balance changes immediately and becomes and remains negative. At the same time the amount of Calcium and inorganic P in the serum falls to 5.05 mgm. and 3.83 mgm. in 100 c.c. respectively, e.g., to less than half the original value.

No. XII, which was given 2 gm. calcium lactate per diem and which during the first 12 periods in spite of a tendency to sink, showed slightly stronger positive balances, presents, with the taking away of the milk powder from the diet, a picture differing from that of the other two animals. Here the phosphorus balance veers immediately to the negative side and remains there, while the amount of inorganic phosphorus in the serum falls to 5.16—6.06 mgm. in 100 c.c. Compared to this, the calcium balance falls, even strongly, and although varying, is to some extent negative. To this the 6.54—6.63 mgm. in 100 c.c. serum existing amount of calcium also corresponds. If No. XII is compared with No. IX of the previous series of experiments, the two animals which both received calcium lactate extra per diem, there is seen in each a lowering of the strongly positive calcium balance present from the commencement. The phosphorus balance differs but slightly.



Table

Date	Dog No. XI. Oatmeal-Milk powder, Lemon juice					Dog Oatmeal-Milk Lemon	
	mgm. Ca in 100 c.c. serum	mgm. P in 100 c.c. serum	Ca balance in gm.	P balance in gm.	Mg. balance in gm.	mgm. Ca in 100 c.c. serum	mgm. P in 100 c.c. serum
1927-8							
13-16/7	10.65	8.65	+ 1.62	+ 1.81		10.65	8.55
25-28/7	10.24	8.88	+ 2.62	+ 2.68		10.24	8.65
6-9/8	9.83	7.80	+ 2.23	+ 1.30		9.42	7.80
18-21/8	9.65	7.61	+ 3.35	+ 2.13		9.29	6.95
24-27/8	9.42	7.27	+ 3.02	+ 1.28		9.01	6.95
11-14/9	7.37	7.27	+ 2.41	+ 1.74		7.37	6.65
23-26/9			+ 1.26	+ 1.69			
5-8/10			+ 1.22	+ 1.79			
17-20/10			+ 0.83	+ 2.26			
29-1/11			+ 0.80	+ 1.36			
10-13/11			+ 0.19	+ 0.98	+ 0.73		
22-25/11	8.73	5.72	+ 1.29	+ 0.93	+ 0.52		
4-7/12 ¹			+ 0.10	+ 0.40	+ 0.77		
16-19/12			- 0.58	- 0.47	+ 0.70		
28-31/12	8.42	4.28	- 1.15	- 0.93	+ 0.44		
9-12/1			- 0.49	- 0.39	+ 0.24		
21-24/1	8.42	4.28	- 0.66	- 0.49	+ 0.28	6.54	5.16
2-5/2	5.05	3.83	- 1.43	- 0.65	+ 0.37	6.63	6.06
14-17/2							

¹ later, oatmeal only.

In the case of No. IX, it lies, so to say, on the same level throughout, and with No. XII, varies somewhat but is clearly positive. Accordingly, when No. XII received a diet of oatmeal only, it was the phosphorus balance which suffered most; it soon became negative and remained so, whereas the calcium balance was positive and negative alternately. It must there-

6.

No. XII. powder + 2 gm. calcium-lactate juice			Dog No. XIII. Oatmeal-milk powder + 5 gm. salt-mixture ($\text{Ca}_3\text{P}_2\text{O}_8 + \text{CaCO}_3$) Lemon juice				
Ca balance in gm.	P balance in gm.	Mg balance in gm.	mgm. Ca in 100 c.c. serum	mgm. P in 100 c.c. serum	Ca balance in gm.	P balance in gm.	Mg balance in gm.
+ 2.28	+ 1.25		10.24	8.00	+ 4.04	+ 2.6	
+ 2.84	+ 1.74		10.24	8.42	+ 3.86	+ 2.37	
+ 1.59	+ 1.09		9.42	7.61	+ 3.66	+ 1.14	
+ 3.99	+ 2.24		9.29	7.27	+ 1.91	+ 1.01	
+ 2.23	+ 1.61		9.42	6.66	+ 3.92	+ 2.97	
+ 2.46	+ 1.71		8.60	8.40	+ 2.66	+ 2.51	
- 0.29	+ 0.74				+ 1.88	+ 3.04	
+ 0.84	+ 0.52				+ 0.89	+ 2.40	
+ 1.81	+ 2.50				+ 0.81	+ 4.31	
+ 1.16	+ 1.36				+ 1.53	+ 2.51	
+ 0.75	+ 0.36	+ 0.17			+ 1.70	+ 2.42	+ 0.47
+ 1.56	+ 1.88	+ 0.44	8.60	8.42	+ 4.26	+ 3.92	+ 0.29
+ 0.46	+ 1.33	+ 0.61			+ 1.23	+ 2.25	+ 0.66
+ 0.29	- 0.96	+ 0.74			+ 0.68	+ 0.57	+ 0.71
- 0.00	+ 0.70	+ 0.42	8.73	5.52	- 0.29	+ 0.51	+ 0.88
+ 0.27	- 0.67	+ 0.19			- 0.42	+ 0.97	+ 0.40
+ 0.15	+ 0.86	+ 0.14	7.94	3.88	- 1.13	+ 0.67	+ 0.47
- 0.89	- 1.25	+ 0.59	6.08	4.21	+ 1.40	+ 1.81	+ 0.89
					+ 0.64	+ 0.84	+ 0.18

fore be said that the supply of calcium lactate is able to hold both calcium and phosphorus balances at a stronger positive level during a rickets-producing diet than is the case without this salt, but it is not able to counteract rickets produced by an oatmeal diet.

Further, as is apparent from Table 6, the magnesium

balances of these animals taken from the 11th period of metabolism onwards, are also included and they are seen to be positive throughout in the case of all animals, even after the deletion of milk powder from the diet. It remains most strongly positive where the phosphorus balance is positive (XIII) but even in cases where the phosphorus balance is negative, and to some extent where the calcium balance is also negative, the magnesium balance is positive as well, although slightly falling.

The experiments in this connection are too brief to risk definite conclusions being drawn, but so much may be said, that *the magnesium balance in the case of experimental rickets is independent of both calcium and phosphorus balance.*

As the magnesium balances of the latter part of the investigations have also been included for the last series of experiments, the results will be discussed further below.

It will be seen when the results of the bone analyses of these animals (Table 7) are approached, that in the case of No. IX which did not receive the extra salt in the diet, the bones have the lowest calcium, phosphorus and magnesium content. This was to be expected, however, as in accordance with the diet it was given, the animal should correspond to the foregoing Nos. V and VII. With No. XII which was given calcium lactate, and No. XIII which was given both $\text{Ca}_3\text{P}_2\text{O}_8$ and CaCO_3 , there are higher values in the bones than with No. XI, but the peculiar situation is found that No. XII has a higher phosphorus content than No. XIII in spite of the latter having been given a super-addition of phosphorus in its diet and having had a phosphorus balance positive throughout, whereas No. XII at the end of the period had a comparatively strong negative balance.

With No. VIII, the «phosphorus» animal, (Table 5) it was found that compared with No. IX, the «calcium» animal, the amount of phosphorus in the bones was least, although No. VIII had a strong phosphorus balance throughout the whole period of experiment.

One should therefore be able to state that the administration of an extra amount of phosphorus in the case of rickets

Table 7.
Bone analyses of rachitic animal (XI), «calcium» animal (XII) and «calcium-phosphorus» animal (XIII).

Dog No.	Bone	% Water & fat	% Ash in		% Ca in			% P in			% Mg in		
			fr. wgt.	dry wgt.	fr. wgt.	dry wgt.	ash	fr. wgt.	dry wgt.	ash	fr. wgt.	dry wgt.	ash
XI.	Femur	67.72	18.41	54.46	6.70	19.82	36.39	3.00	8.86	16.27	0.115	0.341	0.627
	Femur-shaft	61.13	24.28	62.59	9.06	23.31	37.24	3.45	8.89	14.16	0.164	0.422	0.675
XII.	Femur	61.81	20.56	53.85	7.17	18.72	34.89	3.90	8.92	16.57	0.142	0.371	0.688
	Femur-shaft	60.12	24.47	61.60	9.04	22.69	36.93	3.54	8.89	14.47	0.194	0.486	0.792
XIII.	Femur	60.52	22.22	56.46	8.06	20.43	36.20	3.53	7.12	15.88	0.143	0.363	0.643
	Femur-shaft	57.50	26.53	62.38	10.03	23.61	37.85	3.82	8.98	14.40	0.175	0.411	0.658

does not cause any large deposition of phosphorus in the bones of the animals, even if the phosphorus balance is positive.

On the other hand, the administration of a calcium salt seems to cause a greater deposition of calcium in the bones.

Summary:

1. *Tertiary calcium phosphate administered per os must have a beneficial effect on both the calcium and phosphorus balances during experimental rickets but it is not able to counteract its development brought about by a rickets-producing diet.*

2. *Calcium lactate has the same effect as tertiary calcium phosphate.*

3. *Experiments of short duration regarding the Mg-balance show no relationship between this and the calcium or phosphorus balance.*

4. *The administration of phosphoric salt does not give rise to any phosphorus deposition in the bones even if the phosphorus balance is positive.*

5. *The administration of calcium salt seems to cause a larger deposition of calcium in the bones.*

4th Series of Experiments.

Calcium, phosphorus and magnesium metabolism in rickets produced either by oatmeal and skimmed milk powder, wheat flour and skimmed milk powder or by oatmeal only.

As MELLANBY (47) has found that wheat flour has a less harmful influence and has less ability to produce rickets than oatmeal has, the latter in the diet of one animal, No. XVI of this series, was replaced by wheat flour, and, in order to test still further the strong rickets-producing quality of oatmeal, animal No. XVII was put on a diet of this only. As control animal No. XV was used, and it was given the original standard diet of oatmeal and milk powder.

The animals, which were male and of the same litter were taken for experiment when 5 weeks old, after having

Table 8.

[illegible]

been suckled for 4 weeks and having been on an ordinary diet with cod-liver oil for one. The experiment lasted 12 weeks altogether, the animals being killed when 17 weeks old.

After 4 weeks all showed prominent bone symptoms of rickets, which symptoms became much worse during the further progress of the experiment. Both clinically and radiographically, No. XVII, which received oatmeal only, was decidedly the worst. In the case of the other two, the disease was about equally marked, but, radiographically, No. XVI (wheat flour) was the one more seriously attacked. The autopsy similarly showed that this puppy was more affected than No. XV which had received oatmeal and milk powder. There was even a more pronounced swelling of the rib-cartilage junction of No. XV than of No. XVII.

If the results of the investigations regarding the periods of metabolism of these three animals are considered separately, it is striking that in the case of both No. XV and No. XVI the calcium and phosphorus balances are positive the whole time, there being merely the difference that the calcium balances are stronger in the case of No. XVI which was given wheat flour. The opposite is the case, however, where the amount of the two substances in the serum is concerned; in No. XVI it is found to be so low as 5.30 mgm. Ca and 3.07 mgm. inorganic P, per 100 c.c., while with No. XV the lowest amounts are 8.24 mgm. Ca and 4.93 mgm. inorganic P in 100 c.c. serum.

While, therefore, judging from the calcium and phosphorus balances of these animals, the «wheat flour» animal was clinically the most attacked, the «oatmeal» animal (XV) was the most attacked from a chemical point of view.

If negative balances were to be expected in the case of any animal, it should have been in respect of No. XVII which was given an oatmeal diet only, and this proves to be the case, in so far as the calcium balance is negative throughout. On the other hand, the phosphorus balance is weakly positive during the first half of the period of experiment, but veers to the negative side. In spite, however, of these poor balances,

the values of the calcium and inorganic P in the serum are not found to be so low as in the case of No. XVI, as the lowest is 6.79 mgm. Ca and 3.58 mgm. inorganic P in 100 c.c.

In the latter part of the experiment the *magnesium balance* is also included. In the case of dog No. XV which received oatmeal-milk powder, the magnesium balance is clearly positive, corresponding to the positive Ca and P balances. With No. XVI, however, which also has positive Ca and P balances, the magnesium balance is weakly positive, and with No. XVII which was given oatmeal only and which has negative Ca and P balances, the Mg-balance is even a weaker positive, but so much can be said, that it here follows the course of the two other balances and becomes worse when they are negative.

In Table 9 this is again found to be the case where the bone analyses of these animals are concerned, as well as with the normal control animal, a male dog from the same litter of puppies, No. XVIII, which was not included in the experiments but was given an ordinary diet with cod-liver oil added. The amount of Mg. in the bones is lowest in the case of No. XVII which had the weakest balance. It is a little higher in the case of No. XVI which had a somewhat lesser Mg-balance, and is best in the case of No. XV which had a negative balance which was obviously positive. The values of the normal dog No. XVIII are much higher. It is found that, parallel to the negative Ca and P balances of No. XVII, the amount of these substances is also least in the bones of this animal compared with the others. If, however, a comparison is again made of the results of No. XV and No. XVI, where wheat flour replaced oatmeal in the diet, it will be seen that No. XV, which had the worst Ca and P balances, has the least amounts of these substances in the bones. Further, No. XVI which, clinically, was the worst, but had the better balances of these two animals, also shows the larger amounts of calcium and phosphorus in the bones. In this respect, therefore, the result of the bone analyses corresponds in every respect with the result of the investigations into metabolism as *the best balance of an element gives the largest content of that element in the bones.*

Table 9.
Bone analyses of control animal (XVIII), rachitic animal on standard diet (XV), «wheat-flour» animal (XVI) and «oatmeal» animal (XVIII).

Dog. No.	Bone	% Water & Fat	% Ash in		% Ca in			% P in			% Mg in		
			fr. wgt.	dry wgt.	fr. wgt.	dry wgt.	ash	fr. wgt.	dry wgt.	ash	fr. wgt.	dry wgt.	ash
XV.	Femur	75.28	10.40	42.08	3.55	14.36	34.11	1.32	5.33	12.66	0.079	0.32	0.76
	Femur-shaft	70.13	15.78	52.25	5.68	18.80	35.98	1.85	6.13	11.72	0.130	0.43	0.83
XVI.	Femur	73.79	11.91	45.45	4.27	16.31	35.88	1.34	5.15	11.27	0.064	0.24	0.58
	Femur-shaft	63.72	21.89	58.96	8.09	21.79	36.94	2.23	6.01	10.19	0.120	0.32	0.55
XVII.	Femur	81.64	5.31	28.96	1.70	9.24	31.93	0.79	4.32	14.93	0.033	0.13	0.62
XVIII.	Femur	59.99	22.20	55.51	8.00	20.02	36.07	4.02	10.04	18.09	0.150	0.37	0.67
	Femur-shaft	53.93	27.25	59.85	10.16	22.06	36.64	5.80	11.73	19.60	0.170	0.33	0.63

It was stated during the discussion of the values of the Mg-balances discovered in the previous series of experiments that, owing to their short duration, no other conclusion could be drawn from the results than that, in experimental rickets, the magnesium balance is independent of both the calcium and phosphorus balance. It must be permitted to say the same when the results of this series of experiments are viewed. Nor can any legitimate conclusion be drawn here from the relationship of the Mg-balance on the one side and the P-balance on the other. K. MEYER (65) finds in investigations regarding the metabolism of a child having slight rickets, that the Ca and P balances are negative, while the Mg is positive. He maintains, therefore, that MgO does not proceed parallel with CaO.

GASZMANN (66) in an analysis of a rib from a normal child and one from a rickety child, found that while the amounts of Ca and PO_4 were lower in the rachitic rib, the amount of Mg here was larger than in the normal rib. This has not been found anywhere during these experiments.

No further conclusion may be drawn from Mg. investigations of such brief duration, and one could only have been arrived at if the investigations had been undertaken throughout the whole period of experiment.

Summary:

1. *If wheat flour replaces oatmeal in the experimental diet, the animal concerned develops, clinically, the most marked rickets, with the calcium balance stronger and the phosphorus and magnesium balance weaker.*
2. *A diet of oatmeal only produces, clinically, exceptionally pronounced experimental rickets, with negative Ca and P balances, a very low magnesium balance, and small quantities of these substances in the bones.*
3. *Investigations of short duration regarding the Mg-balance merely show that this balance is independent of both the calcium and phosphorus balance.*
4. *The best balance of an element gives the greatest content of this element in the bones.*

Table

Date	Dog No. XIX Oatmeal-meat					Dog No. Oatmeal-meat	
	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca balance in gm.	P balance in gm.	Mg balance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum
1929							
24—27/3			—0.05	—0.13	+ 0.14		
6—9/4			—0.05	—0.33	+ 0.32		
19—22/4	12.8	8.33	+ 0.07	—0.51	+ 0.50	12.8	8.69
2—5/5			+ 0.06	—0.03	+ 0.34		
15—18/5	7.6	2.2	+ 0.01	—0.08	+ 0.22	6.8	4.6
28—31/5			—0.03	—0.02	+ 0.28		
10—13/6	5.5	4.6	—0.13	—0.14	+ 0.09	6.2	6.6

5th Series of Experiments.

Calcium, phosphorus and magnesium metabolism in a rickety animal, a rickety animal with extra supply of calcium, and in a rickety animal with extra supply of phosphorus.

Three puppies, of a mixed breed, were taken for experiment six weeks after birth, after having been suckled for five weeks and having eaten ordinary dog's food for one.

During the experiment the diet consisted of 80 % oatmeal and 20 % raw meat. In addition, each animal received 10 c.c. coconut oil, 5 gm. marmite, and 1.5 gm. NaCl per diem. Moreover, two of the animals received a super-addition of salt in the diet: No. XX received 2 gm. calcium lactate corresponding to 0.26 gm. Ca per diem, and No. XXI received 3 gm. $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ corresponding to 0.52 gm. P per diem.

The development of rachitic bone symptoms here proceeded very rapidly and even $2\frac{1}{2}$ weeks after the commencement of the experiment «rosary» was observed as well as epiphyseal

10.

XX + 2 gm. calcium lactate per diem.			Dog No. XXI Oatmeal-meat and 3 gm. $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ per diem.				
Ca balance in gm.	P balance in gm.	Mg balance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca balance in gm.	P balance in gm.	Mg balance in gm.
+0.55	+0.04	+0.19			-0.04	+0.87	+0.13
+0.46	-0.18	+0.16			-0.12	+0.49	+0.26
+0.72	-0.85	+0.48	9.95	5.13	+0.03	+1.15	+0.42
+0.79	+0.02	+0.48			-0.01	+0.94	+0.19
+0.69	+0.01	+0.47	7.3	5.40	-0.04	+1.12	+0.22
+0.45	-0.31	+0.46			-0.07	+1.06	+0.22
+0.44	-0.37	+0.41	5.0	7.4	-0.05	+1.12	+0.07

swelling of the fore-legs — symptoms which later became more pronounced. After 4 weeks of experiment Nos. XIX and XX both had bowed fore-legs, with convexity outwards. Later, stiffness in the hind-legs developed, likewise difficulty when walking. This was first noticed in the case of No. XXI, but later was more marked in No. XX and most marked in No. XIX which, after 8 weeks of the experiment, had hind-legs so stiff, that, practically speaking, it was unable to walk. After 10 weeks No. XIX was so bad that it complained when its hind-legs were touched and hiccoughed when eating; it became easily irritable, and suffered from cramp in both fore and hind-legs after 11 weeks — a complaint which was observed in the case of No. XXI one week later but in a lesser degree.

If the results of the metabolism investigations are studied (Table 10) it will be found that of these animals No. XIX, which did not receive any super-addition of salt, has the worst balances, both Ca and P, the latter being negative the whole time, while the former tended to keep in the neighbourhood of nil. The animal (No. XX) which received 2 gm. calcium

Table 11.
 Bone analyses of rachitic animal (XIX), with extra supply of calcium (XX) and rachitic animal
 having extra supply of phosphorus (XXI).

Dog. No.	Bone	% Water & Fat	% Ash		% Ca in			% P in			% Mg in		
			fr. wgt.	dry wgt.	fr. wgt.	dry wgt.	ash	fr. wgt.	dry wgt.	ash	fr. wgt.	dry wgt.	ash
XIX.	Femur	77.78	4.51	20.38	1.14	7.08	34.77	0.73	3.29	16.16	0.02	0.10	0.47
	Femur-shaft	80.11	4.51	22.66	1.59	7.98	35.25	0.82	4.19	18.25	0.02	0.11	0.50
XX.	Femur	72.31	10.60	38.27	3.71	13.40	35.02	1.82	6.59	17.21	0.08	0.29	0.76
	Femur-shaft	66.93	17.64	53.96	6.56	19.85	37.19	3.01	9.09	17.04	0.18	0.40	0.76
XXI.	Femur	76.17	8.01	33.63	2.82	11.84	35.23	1.34	6.04	17.37	0.06	0.24	0.72
	Femur-shaft	85.45	14.55	49.57	5.32	18.13	36.58	2.66	9.07	18.29	0.11	0.37	0.74

lactate per diem has, contrary to the other two, an obviously positive Ca-balance while the P-balance almost holds to the negative side. With No. XXI, which received 3 gm. $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ per diem, the relationship is exactly reversed.

Where the Mg-balance is concerned, this shows itself as being obviously strongest positive in the case of the animal (No. XX) which received the calcium lactate, that of the other two animals being weaker, but, all the same, clearly positive. In the 3rd. Series (p. 51) it was found that, according to the brief investigations undertaken, the Mg-balance was almost independent of both Ca and P balances. Moreover, in the bone analyses of the animals of the 2nd. Series it was found that the Mg-quantity in the bones of the animal which received the extra phosphoric salt in its diet, was reduced. Nor was any legitimate relationship found in the 4th Series between the Mg-balance on the one hand and the Ca-balance on the other.

Brief and careful conclusions must also be drawn here where the last series is concerned but it would seem that the Mg-balance depends more on the Ca-balance than on that of P.

On viewing the bone analyses there cannot be found, as was previously the case with No. VIII, any reduced amount of Mg. in the animal which received the super-addition of phosphorus. On the contrary, where the Ca-balance is strongest (No. XX) there is an obvious increase of the amount of calcium in the bones corresponding to the strongest positive Ca-balance of the animals. A similar relationship for the calcium of No. XX cannot be seen for the phosphorus of No. XXI, which received an extra supply of phosphorus and which had the strongest positive P-balance. This has not caused the amount of P in the bones to be greater than in the case of No. XX, where it is the same but it is greater than No. XIX which did not receive any extra supply of salt, either calcium or phosphorus.

Summary:

1. The addition of 2 gm. calcium lactate to a rickets-producing diet causes a positive Ca-balance and a larger amount of calcium in the bones than without the addition of the salt.

2. The addition of 3 gm. $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ per diem to a rickets-producing diet causes a positive P-balance but not a higher amount of P in the bones than that brought about by the addition of calcium.

3. *The Mg-balance seems to a certain degree to be independent of the Ca-balance.* It is otherwise positive even if both Ca and P balances are negative, or one of them positive and the other negative.

C. Discussion of Results.

The results of these experiments cannot be examined to any extent without first treating the question of whether the experimental diet employed is deficient in respect of any one substance vital for the organism.

As previously mentioned the standard diet consisted of skimmed milk powder 20 % and oatmeal 80 %.

The various diet compositions contained from 1.84 to 2.51 % Nitrogen, e.g. a protein content varying from 11.48 to 15.68 %. Therefore, when the animals with a weight at commencement of about 3 kg. ate a minimum of about 200 gm. diet per diem, it may be said that their protein requirements are well covered; this was, moreover, found to be the case in the N-analyses undertaken to correspond with the period of metabolism for the groups of the first two series. See «Register of Experiments» where will be found the results of the N-analyses.

As oatmeal contains from 3.6 to 4.1 % fat and the skimmed milk powder, as it were, nothing, the quantity of fat would have been small if the animals had not received 10 c.c. coconut oil per diem. But 15 to 20 gm. of fat per diem must be considered to be quite sufficient for a puppy of about 3 kg.

In oatmeal alone there is from 63 to 64 % of carbohydrates. To this must be added those contained in the milk powder, so in this respect there is no deficiency in the diet.

Where the mineral substance content of the diet is concerned the amount of calcium, as stated, varied from 0.242 to

0.321 %, an amount which should prove quite sufficient for puppies.

The amount of phosphorus in the diet varied from 0.310 to 0.352 %. If a retention is calculated on the value given by HEUBNER (18) and LIPSCHÜTZ (38), e.g. 0.14 gm. P per kg. of weight of the body per animal — for a dog of 3 kg., 0.42 gm. P per diem — it will be noticed that 200 gm. of diet contains more than sufficient P.

The amount of magnesium in the diet was 0.126 % and therefore should be more than sufficient for a small puppy.

Of other minerals, like Fe, S, Cl, Na, K, etc., quite large quantities are contained in oatmeal, as well as comparatively large quantities in milk powder, so that, even if no direct analyses of these substances have been executed, it may be stated that where these are concerned in the standard diet, a sufficient quantity must be present even for a growing organism. Moreover, 1.5 gm. NaCl per diem was administered extra to the organism.

It should here be observed that, when considering the accessory factors of nourishment, namely vitamins, oatmeal contains sufficient anti-xerophthalmic Vitamin A. No symptoms of xerophthalmia, therefore, have arisen.

Vitamin B was administered to all animals through the medium of yeast extract or marmite.

Owing to the standard diet possessing so large a quantity of oatmeal — which according to MELLANBY (47) is, on its own, of a rickets-producing nature — possibly to its containing an unknown «toxic» substance, the diet must be considered as rickets-producing owing to the lack of the anti-rachitic Vitamin D.

As the purpose was to undertake investigations during the development of experimental rickets and during its florid stage, it was just this matter of ensuring a reliable rickets-producing diet which was wanted and which was obtained in this particular diet.

As previously stated, no mention can be found in any work that dogs can be afflicted by scurvy or by scurvy-like

conditions. The animals of the 1st series were accordingly put upon a rickets-producing diet totally deficient in Vitamin D, as the small amounts which may, perhaps, be found in oatmeal can in this connection be discarded from consideration altogether. Moreover, the diet of this group was also totally deficient in Vitamin C. As the results of the metabolism investigations of this group show variations when compared with those of the next, the conclusion may be permitted that the cause is to be found in the double deficiency of the diet i. e., it is due to the absence of Vitamins C and D. The only animals which during the production of experimental rickets in these investigations showed a negative P-balance both during the development of the disease and during its florid stage are Nos. IV and V, both being animals which lived on a rickets-producing diet lacking Vitamins C and D. Moreover, there was a weak, positive Ca-balance in each case. If a comparison is made between these animals and Nos. VII, XI and XV which received a rickets-producing diet deficient in Vitamin D only, it will be seen that a rickets-producing diet only deficient in that Vitamin will give rise to experimental rickets with a positive P-balance and a negative Ca-balance at the same time.

The conclusion may therefore be drawn that *the absence of Vitamin C in the case of experimental rickets in dogs, although clinically and even microscopically no scurvy or scurvy-like conditions can be proved, must exercise an influence on the mineral metabolism where Ca and P are concerned.*

A reduction of both calcium and inorganic phosphorus in the serum is found and the quantities of the two substances keep parallel with the balances. A similar reduction of both elements in the serum has also been proved by ACKERSON and co-workers (67) in respect of rickety chickens and by SHOHL and BENNETT (54) in the case of rickety dogs. On the other hand, SHIPLEY, MCCOLLUM and co-workers (68) maintain that one form of rickets is characterised by a normal or almost normal calcium and low inorganic phosphorus quantity in the serum and that there is a form with

a low amount of calcium and normal or almost normal inorganic phosphorus. KARELITZ and SHOHL (61) have found that in the case of rickety rats the amount of inorganic phosphorus in the serum falls and that the amount of calcium even rises during the florid stage.

Judging only from the mutual serum relationship of the two substances, it therefore seems that several different forms of rickets can be encountered in the case of animals.

During the production of experimental rickets in puppy No. XVII, which, in contra distinction to the other animals experimented upon, received oatmeal only, the metabolism investigations which revealed negative calcium and phosphorus balances, indicated another form of experimental rickets. The diet was, however, deficient in many respects, Nitrogen in particular. The N-balance was not studied, but had it been, it would certainly have proved for the most part negative.

Many investigators like KOCHMANN (37) and others have found that the phosphorus metabolism is influenced by the assimilation of Nitrogen in the organism. The N-analyses, therefore, should also have been made where the last series is concerned. But as the N-analyses which were made and the results of which are given in the Register of Experiments (page 78—93) in the case of dogs Nos. III—X, did not, in the opinion of the investigator, show any sign of influence on the phosphorus and calcium metabolism respectively, the animals of the last series were weighed only. When the weight graph of No. XVII (fig. 69) is studied it will be seen that the weight of the animal on being killed at 17 weeks old, was only 200 gm greater than it was when taken for experiment at the age of 5 weeks.

Immediately on commencing to treat a rickety puppy (No. IV) with cod-liver oil its *negative phosphorus balance changes rapidly and strongly to the positive side and a calcium balance previously weakly positive, becomes strongly positive*. Further, *the low quantities of the two substances in the serum in that case rise very rapidly to normal values, the phosphorus, however, being more rapid than the calcium*. (See Table 2.)

WILSON (69) maintains that cod-liver oil therapeutics appear to produce the cure of rickets better than its prevention. In the case of the two first series of experiments where a normal control animal in receipt of 10 c.c. cod-liver oil per diem was used to counteract the rickets producing diet, a lesser dose, of, for example, 5 c.c. per diem, judging from the clinical pictures of the high-degree rickets the diet produced, would hardly have been sufficient to keep the control animals normal. The cod-liver oil administered to the rickety animal (No. IV) in a dose of 10 c.c., had a rapid and strong effect, both chemically and clinically.

By adding a calcium salt, a phosphoric salt or a calcium phosphate to the diet, investigations have here been made to discover eventual changes in the calcium and phosphorus metabolism.

In the case of two animals experimented upon (Nos. IX and XII) which received calcium salt in the form of 2 gm. calcium lactate (corresponding to 0.26 gm. Ca per diem) the condition is about equal. The addition is not capable of counteracting the appearance of rickets, but the clinical picture, however, shows the rickets as being less pronounced than in the case of the animals which did not receive the extra calcium salt; parallel with this, it is found that both the calcium and phosphorus balances are stronger in the case of the two «calcium» animals than with animals not having had the extra calcium salt. KARELITZ and SHOHL (61) have found that in a diet containing high calcium and low quantity of phosphorus, where there is a relationship of $\text{Ca} : \text{P} = 1 : 0.235$, both substances have balances that are positive but decreased, and most pronounced where phosphorus is concerned so that not only was there a large, absolute deficiency in the phosphorus retention but a relative one as well. These varying discoveries where rickety puppies and rats are concerned, can, of course, be ascribed to the manner in which the different animals react, but, perhaps, they may also be put down to differences of diet. Oatmeal, according to MELLANBY (47), is itself very rickets-productive owing to its ingredients or to some other

unknown «toxic» substance in it, whereas the diet given to the rats was deficient in vitamin D only. With one animal experimented upon (No. VIII) an addition was made of 2 gm. Na_2HPO_4 corresponding to 0.346 gm. P per diem which gave rise to a clinically much stronger rickets than without the addition of the salt or in cases of animals having had extra calcium salt added to the diet. All the same, the phosphorus balance was better than, and the calcium balance parallel with, that of animals without the addition of salt (VIII).

KARELITZ and SHOHL (61) have found that in rats which received a diet in which the content was Ca:P—1:1 to which was added Na_2HPO_4 , the calcium balance was positive but sinking, and that the phosphorus balance is positive and becomes greater by the addition of Na_2HPO_4 , but in reality, a lesser percentage of the amount of administered phosphorus is retained. During the last week of their experiment they found that the phosphorus retention of the animals was very large. At the same time they found that the addition of phosphate to the diet brought about a strong rise in the amount of inorganic phosphorus in the serum with values up to as much as 16 mgm. in 100 c.c., and a simultaneous fall in the amount of calcium. In the experiments of the present investigator it has been found that, as previously mentioned, with the addition of phosphate there is a fall in the quantities of both calcium and inorganic phosphorus in the serum.

It appears, therefore, that it is difficult, off hand, to make comparisons between experiments with rickets in the case of puppies and rickets in the case of rats. This applies not only where calcium salt is concerned, but also with regard to the effect of phosphoric salt if it is unknown whether the two types of animals react the same, or whether the whole difference can be ascribed to the difference in diet.

Dealing now with what has been found by the extra addition of a large dose of tertiary calcium phosphate per diem (No. XIII), this addition gave a large calcium and phosphorus balance but in the experimental diet used it was not able to counteract the development of rickets. In this case, however, an extra CaCO_3

per diem was added so that the effect cannot be ascribed to the amount of phosphorus alone, especially when is taken into consideration what has previously been mentioned and found with regard to the administration of extra calcium salt giving rise to stronger calcium and phosphorus balances.

All the same, it is difficult to imagine that the relatively small amount of calcium in the form of CaCO_3 , only 0.194 gm. per diem, by comparison with the amount of calcium in the diet on the one hand and the amount of tertiary calcium phosphate (corresponding to 1.818 gm. Ca per diem) on the other, should have so great an effect. Even if, for the first metabolism period only, the calcium retained from tertiary calcium phosphate can be calculated, that is not to say that the same could not occur later on during the experiment. The experiments mentioned by R. BERG (63) and by ORR and co-workers (57) do not prove that tertiary calcium phosphate cannot be resorbed so long as no attempt is made during the investigations to determine the hydrogen-ion concentration both in the ventricle and intestines during the period of digestion.

During the latter half of the three final series of experiments the magnesium balance of the animals has also been included. These were of too short duration to permit of any other conclusion being arrived at from the results obtained than that the *magnesium balance shows no relationship to either the calcium or phosphorus balance.* (See tables 6, 8 and 10.)

By the replacement in the experimental diet of oatmeal by wheat flour a clinically stronger rickets was produced, while, on the other hand, the calcium and phosphorus balances were better, something which also found expression in the composition of the bones, the bones of the «wheat flour» animal containing more calcium and just as much phosphorus as those of the corresponding «oatmeal» animal (No. XV).

If, however, a diet is given of oatmeal only, except-ionally strong rickets, clinically, is produced, with negative calcium and phosphorus balances and low magnesium balance

and, something which is not surprising when the results of the bone analyses are studied, even a spontaneous fracture.

A diet of oatmeal only, however, is deficient in many respects so that here many factors play a part; but the microscopical picture of the bones of this animal showed the same rachitic picture as its brother of the same litter which was given the original standard experimental diet, only the changes were stronger and more pronounced.

Where the composition of the bones is concerned it is seen that in experimental rickets in the case of dogs, a marked increase of the water and fat content is found as well as an increase in the quantity of the organic ingredients; there is at the same time a very low content of both calcium and phosphorus in fresh and dry weight. (See Tables 3, 5, 7, 9 and 11.) The quantity of calcium and phosphorus in the bone ash, on the contrary, differed very little in the case of healthy and ill animals. That the calcium and phosphorus in the bones is reduced has, as previously mentioned, also been found to be the case by GASZMANN (66) in respect of a rachitic rib of a child. DUTCHER and co-workers (70) found a marked reduction of the ash content in the femur ash of rachitic rats. SCHABAD (33) has also found that the relationship between ash and organic substance in dried rachitic bones is as 20:80 as against 60:40 in normal bones. He has further found that the calcium content falls while the phosphorus content rises so that a relationship appears of Ca:P—100:70—75 against normal 100:78—85. KORENCHEVSKY and CARR (71) have also found in rachitic rats an increase of the amount of water in the bones as well as a decrease of the amount of calcium of both fresh and dry weight. The results obtained, therefore, in the case of these rickety puppies, correspond to what other investigators have found. It may accordingly be said that *in the bones of rachitic puppies there is an increase of the water content and of the organic ingredients and a decrease in quantity of both calcium and phosphorus.*

The super-addition to the diet of calcium salt, which had a relatively good effect on both the calcium and phosphorus

balance, (Nos. IX and XII) also shows where the composition of the bones is concerned, as having exercised a beneficial influence, as the quantities of both *calcium and phosphorus in the bones have increased* when compared to those of the animal which did not receive the calcium salt.

As against this it is seen that, by the super-addition of Na_2HPO_4 to the diet, (Animal No. VIII) the amount of phosphorus in the bones, in spite of the higher phosphorus balance of the animal which received the addition of salt, is unchanged, and that the calcium and magnesium amounts in the bones are even smaller. This supports the clinical observation that the «phosphorus» animal was the one most severely attacked by the disease.

Finally, there are the results obtained by the large doses of $\text{Ca}_3(\text{PO}_4)_2$ — CaCO_3 mixture (No. XIII). It is found here that the amount of calcium in the bones is somewhat higher, and the amount of phosphorus the same, in comparison with the amounts in the bones of animal No. XI which did not receive the addition of salt; the quantity of calcium is a little higher, but that of phosphorus a little lower, than in animal No. XII which was given the calcium lactate. This fact that, by the administration of tertiary calcium phosphate, no larger, or equally large quantities of phosphorus in the bones are obtained than by the administration of the calcium salt alone, does not deny that calcium is not resorbed by the tertiary calcium phosphate. Where the phosphorus is concerned, there is the analogy of the animal which received Na_2HPO_4 thereby having a larger phosphorus balance and an unchanged quantity of phosphorus in the bones in comparison with the animal which did not have the phosphoric salt addition in the diet.

Coming now to the consideration of the difference between oatmeal and wheat flour investigated during the final series of experiments, there was, clinically, a worse, but judging from the calcium and phosphorus balances, a lesser, pronounced rickets in the case of wheat flour. Where the *bones* are concerned, *the ash and calcium content is larger in the case of*

wheat flour while the phosphorus content in the dry weight, and in the ash, is less; the same applies to the magnesium content.

If, on the other hand, oatmeal is given exclusively (No. XVII) there is obtained a, clinically, heavy rickets, with negative balances and marked reduction of calcium, phosphorus and magnesium in the bones, there being at the same time a marked increase in the water content and of the organic ingredients.

A one-sided oatmeal diet, therefore, is an exceptionally deficient diet for a growing organism.

Viewed as a whole the bone analyses show that where there is the best balance of an element, calcium or phosphorus, there is also the largest content of that element in the bones.

D. Summary.

During the investigations regarding experimental rickets it was found that:

1) Owing to the lack of both Vitamin C and D in the diet

there is a negative phosphorus balance and a weak positive calcium balance turning negative.

2) When Vitamin C only is lacking in the diet

the calcium balance is poorer than with the addition of lemon juice.

It is therefore not improbable that when dogs, at an early stage are put on a diet lacking Vitamin C they can be afflicted by scurvy or by a scurvy-like condition, a disease in dogs where the changes undergone in metabolism have not hitherto been investigated.

Cod-liver oil cures experimental rickets very rapidly, both chemically and clinically. The negative or weak positive balances quickly become strongly positive.

3) When Vitamin D is lacking in the diet:

a) *thus a form of rickets proper in dogs, a positive phosphorus balance and a negative calcium balance is found.*

b) Na_2HPO_4 added extra to the diet gives rise to clinically worse rickets but to a better phosphorus balance and parallel calcium balance than without the addition.

c) Calcium lactate added extra to the diet gives rise to a clinically lesser pronounced rickets, with stronger calcium and phosphorus balances. Moreover, there is a greater calcium content in the bones.

d) A salt mixture of $\text{Ca}_3(\text{PO}_4)_2$ and CaCO_3 (relationship 840:95) brings about greater calcium and phosphorus balances than without the addition of the salt mixture.

e) Wheat-flour, compared with oatmeal, produces clinically severer rickets, weaker phosphorus and magnesium balances but a stronger calcium balance.

f) According to the balances of the elements concerned, the amount of calcium and inorganic phosphorus in the serum is lowered, in some cases very considerably.

4) *The magnesium balance is independent of both the calcium and phosphorus balances.*

5) The best balance of an element gives as a rule the greatest content of that element in the bones.

6) On a diet which is extremely insufficient for a growing organism, *oatmeal only*, a diet deficient in Vitamin D and in Nitrogen in particular, *a much stronger rickets is produced with negative calcium, phosphorus and magnesium balances.*

E. Register of Experiments.

1st. Series of Experiments.

A litter of mongrels consisting of 5 dogs, referred to in the register as Nos. I—V, Nos. I and II being female, the others male.

The puppies were born 21/9/25, were suckled for 5 weeks (until 4/11) and were then given maize and oatmeal porridge with unskimmed and skimmed milk with bread for 2 weeks. On 6/11 and 9/11 they were given 20 and 25 c.c. cod-liver oil respectively. On 11/11 they were put on a rickets-producing diet, consisting of:

skimmed milk powder	20 %
oatmeal	80 %

and distilled water.

No. I — received 10 c.c. coconut oil per diem

» II — » 10 » cod-liver oil » » Control animal for No. I

» III — » 10 » » » » » » » » » » » » »

Nos. IV—V

» IV — » 10 » coconut oil

» V — » 10 » » »

In addition, each received 5 gm. marmite and 1.5 gm. NaCl per diem.

I. Female.

11/11/25 (7 weeks old) Wgt. 4600 gm.

Ca 16.37	} mgm. in 100 c.c. serum.
P 8.00	

26/11/25 Slight swelling of the distal ulna and radius epiphyses. A slight «Rosary».

30/11/25 X-Rays: Increased epiphyseal cartilage.
Swollen distal radius epiphyseal cartilage.

1/12/25 (10 w.o.) w. 5300 gm.

Ca 9.26	} mgm. in 100 c.c. serum.
P 7.08	

Increasing epiphyseal swelling and «Rosary».
Eats well.

14/12/25 (12 w.o.) w. 6200 gm.

Ca 6.88 }
P 6.38 } mgm. in 100 c.c. serum.

Fore-legs very bowed, and epiphyseal swelling. The position of the wrist joints resembles a subluxation. «Rosary» increasing.

19/12/25 X-Rays: Great increase of epiphyseal cartilage. Large epiphyseal swelling. Concave and serrated epiphyses.

28/12/25 w. 6550 gm.

Ca 6.64 }
P 5.48 } mgm. in 100 c.c. serum.

Very quiet. Legs very bowed.

6/1/26. (17 w.o.). During the last 8 days, walking has been difficult; has not been able to raise itself on hind legs. Moans even when carefully put down. This evening, suddenly, tetanic cramp in all extremities, also opisthotonus.

Ca 6.39 }
P 4.20 } mgm. in 100 c.c. serum, one hour after the tetanic attack.

X-Rays: Marked increase of concave, serrated epiphyseal cartilage. Considerable epiphyseal swelling.

7/1/26. w. 6900 gm.

Ca 6.22 }
P 4.00 } mgm. in 100 c.c. serum.

To-day, tetanic trembling in the extremities is easily caused, merely by touching the animal inadvertently. Has difficulty in moving the front legs, drags itself forward by the help of these, with hind part of body trailing after. The epiphyseal swelling on the fore legs is very marked.

9/1/26. w. 6400 gm.

Ca 6.10 }
P 4.00 } mgm. in 100 c.c. serum.

Has not eaten anything during the last 36 hours. To-day raises itself with great difficulty on its hind legs and stumbles a few paces, moaning constantly. Trembling in whole of body.

10/1/26. During the last 24 hours has eaten 400 gm. food. Apparently improved to-day. Does not walk more than a few paces. Trembling over the whole of the body.

12/1/26. w. 6600 gm.

Ca 6.94 }
P 4.10 } mgm. in 100 c.c. serum.

13—15/1/26. Metabolism Period.

Weight: no change.

Ca-balance — — 0.476 gm. Ca.

P. " — + 0.404 " P.

1/18/26. Ca 7.49 }
P 4.96 } mgm. in 100 c.c. serum.

Cannot raise itself on hind legs.

Sits and passes water.

22/1/26. (19 w.o.) w. 6550 gm.

Ca 7.31 }
P 4.00 } mgm. in 100 c.c. serum.

22—24/1/26. Metabolism Period.

Increase in weight: 250 gm.

Ca-balance — — 0.181 "

P. " — + 0.764 "

28—30/1/26. Metabolism Period.

Increase in weight: 150 gm.

Ca-balance — + 0.035 "

P. " — + 1.764 "

2/2/26. X-Rays: Great increase of concave and serrated epiphyseal cartilage. Large epiphyseal swelling. Bowed fore-legs.

3/2/26. Intravenous injection of 1 gm. CaCl_2 .

	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum.
Before the injection:	7.78	4.48
1/4 hour after inj.	13.10	4.64
1 " " "	10.81	4.04
3 hours " "	7.86	5.08
7 1/2 " " "	6.11	4.60
10 " " "	6.21	4.00
24 " " "	6.11	4.20

4/2/26. (20 w.o.). Has been on a rickets-producing diet for 12 weeks. Killed.

Result of Autopsy:

No sub-cutaneous fat.

Thorax: round, barrel-shaped. On the inside strongly marked swelling of the costo-chondral junction is seen. On cutting through the junction is seen to be uneven, serrated.

Tibia: the proximal epiphyseal cartilage 4 mm. broad, uneven, serrated.

Bowed fore-legs, as well as a pronounced swelling of the distal epiphysis.

The bones are soft, easily cut through.

II. Female:

11/11/25. (7 w.o.) wgt. 3200 gm.

Rickets-producing diet + 10 c.c. cod-liver oil per diem.

24/11/25. (9 w.o.) w. 4350 gm.

Ca 10.41 }
P 8.18 } mgm. in 100 c.c. serum.

26/11/25. No epiphyseal swelling or «Rosary». Lively.

30/11/25. X-Rays: Decreased epiphyseal cartilage. No swelling of the distal radius epiphysis.

1/12/25. (10 w.o.) w. 4950 gm.

Ca 10.60 }
P 8.60 } mgm. in 100 c.c. serum.

Bones normal.

14/12/25. (12 w.o.) w. 6550 gm.

Ca 10.60 }
P 8.87 } mgm. in 100 c.c. serum.

Bones normal. Eats well. Lively.

19/12/25. X-Rays: Decreased epiphyseal cartilage, no serration. No epiphyseal swelling.

28/12/25. w. 8200 gm. Very lively.

6/1/26. (17 w.o.) X-Rays: As 19/12/25.

8/1/26. w. 9450 gm.

Ca 10.68 }
P 8.00 } mgm. in 100 c.c. serum.

Eats about 500 gm. food per diem.

12/1/26. w. 10,050 gm.

22/1/26. (19 w.o.) w. 11,300 gm.

Ca 10.41 }
P 8.24 } mgm. in 100 c.c. serum.

2/2/26. X-Rays: Decreased, straight epiphyseal cartilage. No epiphyseal swelling. Legs straight.

3/2/26. (20 w.o.) w. 12,800 gm.

Ca 10.40 }
P 8.52 } mgm. in 100 c.c. serum.

Bones normal.

8/2/26. w. 13,400 gm.

Killed.

Result of Autopsy:

Much sub-cutaneous fat.

Thorax: Deep. On the inside an almost imperceptible swelling just marking the junction between the rib-bone and cartilage.

On cutting through the costo-chondral junction this is seen to be rectilineal, even. On cutting through, all bones are found to be hard.

The epiphyseal cartilage of the various bones, narrow, even.

Dog No. III.

Date	Weight bal- ance in gm.	N				Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca			
		Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.			Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1925-6											
12-15/11		14.01	6.80	4.18	+ 3.08	10.65	8.00				
19-21/11	+ 350	20.16	2.00	6.65	+ 11.51	10.55	8.32				
26-28/11	- 200	14.63	6.82	2.27	+ 6.04	10.60	8.28	1.16	0.05	0.66	+ 0.45
1-3/12	+ 120	24.13	6.79	6.72	+ 10.62	10.71	8.72	2.51	0.06	1.12	+ 1.33
5-7/12	+ 100	27.57	10.85	6.72	+ 10.00	10.50	8.52	2.91	0.07	1.26	+ 1.58
10-12/12	+ 300	24.56	14.49	6.18	+ 3.89	10.68	8.74	2.50	0.06	1.38	+ 1.06
16-18/12	0	26.28	13.90	8.23	+ 4.15	10.60	8.28	2.62	0.03	0.47	+ 2.12
20-23/12	+ 450	30.20	12.85	9.25	+ 8.10	10.20	8.78	2.91	0.04	0.82	+ 2.05
28-31/12	0	31.17	18.43	9.16	+ 3.58	10.76	8.81	3.68	0.02	0.90	+ 2.76
4-7/1	+ 100	32.36	12.64	10.75	+ 8.97	10.42	8.65	3.17	0.03	1.21	+ 1.93
10-13/1	0	28.66	14.65	10.15	+ 3.86	10.80	8.88	2.93	0.04	0.68	+ 2.21
16-19/1	+ 650	40.15	13.65	16.40	+ 10.10	10.05	8.68	4.13	0.06	1.10	+ 2.97
22-25/1	+ 850	46.00	13.10	21.22	+ 11.68	10.50	8.32	4.73	0.02	1.74	+ 2.97
28-31/1	+ 600	50.59	19.48	26.76	+ 4.35	10.46	8.64	5.17	0.02	1.94	+ 3.21
3-6/2	+ 650	50.37	17.95	12.41	+ 20.01	10.48	8.88	5.44	0.05	2.03	+ 3.36
9-12/2	+ 400	42.94	12.10	18.51	+ 12.33	10.85	8.60	5.34	0.02	1.66	+ 3.66
15-18/2	+ 500	39.52	12.39	25.90	+ 1.23	10.72	8.60	5.35	0.02	1.32	+ 4.01
21-24/2	+ 750	46.20	18.82	17.02	+ 10.36	10.68	8.40	5.60	0.03	1.16	+ 4.41
27/2-2/3	+ 1050	54.62	14.03	24.64	+ 15.90	10.64	8.60	5.48	0.02	1.77	+ 3.69
5-8/3	+ 500	50.61	22.22	18.16	+ 10.23	10.56	8.40	5.31	0.01	1.68	+ 3.62

Male.

P				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				¹¹ / ₁₁ . W. 3000 gm.
1.98	0.57	1.89	+ 0.01	²⁰ / ₁₁ 25. No epiphyseal swelling or «Rosary».
3.75	0.71	1.67	+ 1.37	³⁰ / ₁₁ 25. X-Rays: Decreased epiphyseal cartilage. No swelling of the epiphyses.
4.02	1.22	2.31	+ 0.49	
3.35	0.26	2.40	+ 0.69	¹⁴ / ₁₂ 25. W. 7150 gm. Bones normal.
3.85	0.88	3.63	- 0.66	¹⁹ / ₁₂ 25. X-Rays: Narrow epiphyseal cartilage. No epiphyseal swelling.
4.81	0.77	2.33	+ 1.71	
5.08	1.12	2.98	+ 1.58	²⁸ / ₁₂ 25. W. 9700 gm. Bones normal. Eats much.
4.51	1.01	2.82	+ 0.68	⁷ / ₁ 26. W. 10,600 gm.
4.41	0.88	2.72	+ 0.81	
5.76	0.74	4.34	+ 0.68	²⁰ / ₁ 26. X-Rays: Narrow epiphyseal cartilage. Good deposit of chalk.
6.60	0.66	5.38	+ 0.56	²⁸ / ₁ 26. W. 12,150 gm.
8.45	0.42	6.24	+ 1.79	
8.16	0.56	3.75	+ 3.85	² / ₂ 26. W. 14,400 gm. X-Rays: Narrow, straight epiphyseal cartilage. No epiphyseal swelling. Legs straight.
6.83	0.07	5.58	+ 1.18	
6.53	0.23	3.90	+ 2.40	
6.86	0.18	4.40	+ 2.28	²⁷ / ₂ 26. W. 16,400 gm.
8.16	0.09	2.89	+ 5.18	³ / ₂ 26. X-Rays: as ² / ₂ 26.
8.03	0.15	4.26	+ 3.62	³ / ₂ 26 (24 weeks old). W. 17,600 gm. On diet for 17 weeks. Bones normal. Killed.

Autopsy. Thorax: Deep. On the inside no swelling of the costochondral junction. The junction is straight and even.

The bones are large, hard. Epiphyseal cartilage narrow, $\frac{1}{2}$ —1 mm. broad, even and straight.

Dog No. IV.

Date	Weight bal- ance in gm.	N				Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca			
		Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.			Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1925--6											
12--15/11		14.01	7.28	4.28	+ 2.75	10.65					
19--21/11	+ 500	16.42	2.02	7.28	+ 7.12	10.37	8.12				
26--28/11	+ 100	14.68	5.26	4.34	+ 5.08	10.15	7.65	1.16	0.02	0.61	+ 0.53
1--3/12	+ 300	20.32	5.75	5.81	+ 8.76	9.26	7.20	2.11	0.09	1.22	+ 0.80
5--7/12	+ 650	27.57	9.11	11.58	+ 6.86	9.12	6.80	2.91	0.05	1.81	+ 1.05
10--12/12	+ 600	19.65	4.60	11.31	+ 3.74	8.92	6.48	2.01	0.05	1.94	+ 0.02
16--18/12	+ 250	16.72	4.27	9.32	+ 3.13	7.17	6.80	1.70	0.02	0.65	+ 1.03
20--23/12	+ 150	18.58	5.33	8.36	+ 4.89	7.24	7.88	1.83	0.03	1.79	+ 0.01
28--31/12	+ 50	15.59	2.81	5.98	+ 6.80	6.98	7.42	1.76	0.02	1.19	+ 0.55
4--7/1	+ 300	17.43	4.04	11.19	+ 2.20	7.50	6.15	1.88	0.01	2.30	- 0.43
10--13/1	+ 350	23.89	5.92	12.54	+ 5.43	6.58	5.68	2.46	0.06	1.98	+ 0.42
16--19/1	0	27.60	11.50	13.50	+ 2.60	9.14	8.40	2.87	0.02	1.21	+ 1.63
22--25/1	+ 250	18.16	8.18	4.30	+ 5.68	9.14	8.08	2.78	0.02	0.97	+ 1.79
28--31/1	+ 200	23.10	8.83	12.05	+ 2.22	10.46	8.60	2.41	0.04	0.84	+ 1.52
3--6/2	+ 350	24.11	7.77	8.71	+ 7.63	10.81	8.16	2.65	0.05	0.79	+ 1.81
9--12/2	+ 400	24.87	6.43	9.67	+ 8.82	10.76	8.76	3.13	0.02	0.61	+ 2.50
15--18/2	+ 150	34.32	6.50	14.70	+ 13.12	10.48	8.00	4.66	0.01	0.78	+ 3.87
21--24/2	+ 600	35.27	3.37	11.85	+ 20.05	10.42	8.68	4.29	0.04	0.66	+ 3.59
27/2--2/3	+ 450	38.69	10.06	15.10	+ 13.53	10.48	8.60	3.91	0.04	0.87	+ 3.01
5--8/3	+ 400	36.44	6.69	18.23	+ 11.52	10.48	8.32	3.85	0.02	1.09	+ 2.74

Male.

P				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				¹¹ / ₁₁ 25. W. 2900 gm.
1.97	0.19	1.77	+0.01	²⁰ / ₁₁ 25. No epiphyseal swelling or «Rosary».
3.16	0.91	1.76	+0.49	³⁰ / ₁₁ 25. X-Rays: Increase of epiphyseal cartilage. Slight swelling of the distal radius epiphysis.
4.03	0.50	3.83	-0.41	
2.68	0.22	3.60	-1.14	¹⁴ / ₁₂ 25. W. 6000 gm. Prominent epiphyseal swelling of front legs, with curvature of these, also position resembling subluxation of wrist joints.
2.47	0.57	2.53	-0.66	¹⁰ / ₁₂ 25. X-Rays: Great increase of epiphyseal cartilage. Obvious epiphyseal swelling. Concave and serrated epiphyses.
2.91	0.67	2.93	-0.69	²⁰ / ₁₂ 25. W. 6350 gm. Marked curvature of front legs. Epiphyseal swelling increased.
2.38	0.48	1.78	+0.12	⁷ / ₁ 26. W. 6900 gm.
2.65	0.67	3.06	-1.09	¹⁰ / ₁ 26. 10 c.c. cod-liver oil instead of 10 c.c coconut oil.
3.68	0.68	3.65	-0.65	²⁰ / ₁ 26. X-Rays: Epiphyseal cartilage as ⁷ / ₁ 26, but definite, narrow chalk-deposit zone.
3.97	0.45	3.41	+0.11	²² / ₁ 26. W. 7650 gm.
3.84	0.61	2.44	+0.79	
3.88	0.82	3.30	-0.24	
3.92	0.63	2.35	+0.94	² / ₂ 26. W. 7800 gm. X-Rays: Decreased, slightly uneven epiphyseal cartilage. Obvious epiphyseal swelling. Bowed legs.
3.97	0.35	2.37	+1.25	
5.68	0.16	3.59	+1.93	
5.24	0.26	2.86	+2.12	²⁴ / ₂ 26. W. 10150 gm.
5.79	0.31	3.85	+2.18	⁸ / ₂ 26. X-Rays: Decreased, even, epiphyseal cartilage. Epiphyseal swelling decreased. Bowed legs. Good deposit of chalk.
5.79	0.38	4.55	+0.86	¹² / ₂ 26. (24 w.o.) W. 10,200 gm.

Autopsy. Thorax: Round. On the inside slightly pronounced serration of the costo-chondral junctions, which on being cut through found to be almost quite even and straight. Bones hard. Epiphyseal cartilage narrow 1—1½ mm., somewhat unevenly serrated.

Date	Weight bal- ance in gm.	N				Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca			
		Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.			Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1925-6											
12-15/11		14.01	7.40	3.51	+ 3.10	10.60	8.00				
19-21/11	+ 20	15.15	3.56	4.01	+ 7.57	10.55	8.32				
26-28/11	- 50	14.63	3.62	4.98	+ 6.03	10.35	7.92	1.16	0.08	0.71	+ 0.37
1-3/12	+ 100	21.57	3.85	9.27	+ 8.45	10.74	7.68	2.24	0.03	1.88	+ 0.83
5-7/12	+ 350	27.57	7.82	11.34	+ 8.41	10.00	6.48	2.91	0.07	1.88	+ 0.96
10-12/12	+ 500	19.65	6.53	8.70	+ 4.42	10.23	6.72	2.02	0.07	1.87	+ 0.08
16-18/12	- 300	16.72	12.52	10.54	- 6.34	7.54	6.24	1.70	0.03	1.13	+ 0.54
20-23/12	0	16.26	10.69	7.95	- 2.38	9.19	6.68	1.61	0.02	1.61	- 0.02
28-31/12	+ 100	21.58	4.51	9.74	+ 7.33	7.72	5.64	2.40	0.02	1.93	+ 0.45
4-7/1	- 100	17.43	4.95	11.65	+ 0.83	8.42	5.34	1.68	0.02	2.10	- 0.44
10-13/1	+ 200	21.50	7.55	9.03	+ 4.92	6.98	4.68	2.22	0.01	1.73	+ 0.48
16-19/1	- 50	20.07	7.35	10.55	+ 2.17	9.14	6.04	2.11	0.01	0.89	+ 1.21
22-25/1	- 100	25.42	7.65	17.90	- 0.13	7.76	4.76	2.66	0.03	2.83	- 0.20
28-31/1	- 400	18.58	8.29	9.95	+ 0.34	7.28	5.48	1.86	0.03	1.81	+ 0.02
3-6/2	0	24.11	7.57	12.30	+ 4.24	6.98	4.84	2.65	0.03	2.41	+ 0.21
9-12/2	+ 300	20.34	10.28	5.32	+ 4.74	7.42	4.80	2.57	0.02	2.48	+ 0.07
15-18/2	+ 250	34.32	6.73	14.62	+ 12.97	6.98	4.60	3.14	0.02	3.17	- 0.05
21-24/2	+ 200	19.85	7.73	9.67	+ 2.45	6.98	4.20	2.44	0.05	2.22	+ 0.17
27/2-2/3	+ 450	22.77	5.03	12.28	+ 5.41	6.80	4.12	2.34	0.04	2.99	- 0.69
5-8/3	0	18.22	4.13	13.50	+ 0.59	6.76	4.00	1.97	0.02	3.03	- 1.08

Male.

P				Remarks
Total intake	gm. in urine	gm. in feces	Balance in gm.	
				¹¹ / ₁₁ 25. W. 3000 gm.
1.97	0.67	1.50	-0.20	²⁶ / ₁₁ 25. W. 4700 gm. Slight swelling of the distal ulna and radius epiphyses. Slight «Rosary».
3.36	0.59	2.32	+0.45	³⁰ / ₁₁ 25. «Rosary» apparent. X-Rays: Increased epiphyseal cartilage. Some swelling of the distal radius epiphysis.
4.03	0.97	3.33	-0.28	¹⁴ / ₁₂ 25. W. 6900 gm. Pronounced «Rosary» and epiphyseal swelling.
2.69	0.23	3.61	-1.16	¹⁹ / ₁₂ 25. X-Rays: Greatly increased epiphyseal cartilage. Obvious epiphyseal swelling. Concave and serrated epiphyses.
2.47	0.61	3.08	-1.23	
2.55	0.42	2.83	-0.70	
3.38	0.69	3.22	-0.53	²⁸ / ₁₂ 25. W. 7750 gm. The epiphyseal swelling has grown considerably. The fore-legs are very bowed. Walking very difficult.
2.65	0.52	3.50	-1.37	⁷ / ₁ 26. W. 8150 gm.
3.41	0.45	2.96	-0.00	
2.90	0.44	2.91	-0.45	²⁰ / ₁ 26. X-Rays: The epiphyseal cartilage as on ⁷ / ₁ 26. No chalk-deposit zone as with No. IV. Considerable curvature of ulna and radius.
3.66	0.54	4.11	-0.99	²² / ₁ 26. W. 9200 gm.
2.96	0.55	3.34	-0.93	
3.92	0.58	4.08	-0.74	² / ₂ 26. W. 9450 gm. X-Rays: Very greatly increased, very concave and serrated epiphyseal cartilage. Large epiphyseal swelling. Curvature of ulna and radius.
3.26	0.38	3.72	-0.84	
3.80	0.28	4.40	-0.88	
2.96	0.29	2.92	-0.25	²⁴ / ₂ 26. W. 9550 gm.
3.42	0.12	3.60	-0.30	⁸ / ₂ 26. X-Rays: Ulna and radius as ² / ₂ 26.
2.97	0.13	4.02	-1.18	⁹ / ₂ 26. Killed.

Autopsy: Thorax: Showed on the inside an exceptionally prominent swelling of the costo-chondral junctions, which on being cut through proved to be very irregularly serrated. All bones very soft and easy to cut through. The epiphyseal cartilage broad and unevenly serrated.

2nd. Series of Experiments.

A litter of puppies (pure Norwegian elk-hound breed) consisting of 5 dogs, Nos. VI—X, of which Nos. VIII and IX were male, the others female.

The animals were born $^{11}/_5$ 26, were suckled for 6 weeks and received, with the exception of No. X, maize-oatmeal porridge, a little bread and skimmed-milk + 1 child's spoonful of cod-liver oil per diem for 2 weeks, until $^4/_5$ 26, when, 8 weeks old, they were put on rickets-producing diet as before.

No. VI received 10 c.c. cod-liver oil per diem. Control animal.

Dog No. VI.

Date	Weight balance in gm.	N				Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca			
		Total intake	gm. in urine	gm. in faeces	Balance in gm.			Total intake	gm. in urine	gm. in faeces	Balance in gm.
1926											
8—11/5	+ 350	20.51	5.85	5.66	+ 9.00	10.16	8.41	2.06	0.01	0.85	+ 1.20
14—17/5	+ 350	20.51	6.86	5.71	+ 7.94	10.16	8.69	2.21	0.03	1.09	+ 1.09
20—23/5	+ 850	29.65	9.89	8.68	+ 11.58	10.39	8.75	4.07	0.02	1.04	+ 3.01
26—29/5	+ 600	33.60	13.76	10.34	+ 9.50	—	8.69	4.62	0.05	1.54	+ 3.03
1—4/6	— 150	24.05	12.95	8.86	+ 2.24	10.65	8.69	3.21	0.11	1.60	+ 1.50
7—10/6	+ 250	30.07	12.34	9.71	+ 8.02	10.16	8.28	4.14	0.06	1.80	+ 2.28
13—16/6	+ 250	34.85	14.92	9.13	+ 10.80	10.16	8.05	5.45	0.05	2.67	+ 2.73
19—22/6	+ 300	34.85	19.01	10.73	+ 5.11	10.16	8.00	5.45	0.05	2.47	+ 2.93
25—28/6	+ 700	38.72	24.58	9.87	+ 4.37	10.38	8.12	5.90	0.07	2.52	+ 3.31
1—4/7	+ 700	36.79	19.16	9.80	+ 7.83	10.16	8.12	5.61	0.15	2.32	+ 3.13
7—10/7	+ 200	29.45	15.62	9.10	+ 4.73	—	—	4.60	0.04	2.68	+ 1.88
13—16/7	— 650	9.19	13.14	—	— 3.95	10.16	8.42	1.44	0.03	0.75	+ 0.66
25—28/7	+ 250	39.56	15.13	6.52	+ 17.91	10.68	8.00	5.28	0.04	3.13	+ 2.11
31/7—3/8	+ 500	41.54	18.76	8.98	+ 13.80	—	—	5.55	0.05	3.73	+ 1.77
6—9/8	+ 650	43.56	20.21	8.70	+ 14.65	10.68	8.00	6.43	0.03	2.91	+ 3.49
12—15/8	+ 900	45.46	25.29	8.63	+ 11.54	10.68	8.20	6.71	0.09	5.73	+ 0.89
18—21/8	+ 150	38.72	21.63	9.59	+ 7.50	10.19	8.20	5.90	0.06	4.44	+ 1.40
24—27/8	+ 400	38.72	19.91	7.78	+ 11.03	10.68	8.60	5.90	0.06	3.00	+ 2.84
30/8—2/9	+ 850	40.66	22.61	5.98	+ 12.07	10.68	8.20	6.20	0.07	3.53	+ 2.60

Dog No. VII.

Date	Weight bal- ance in gm.	N				Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca			
		Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.			Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1926											
8—11/5	+ 450	18.45	3.89	7.32	+ 7.24	10.65	8.48	1.99	0.01	0.76	+ 1.22
14—17/5	+ 300	18.45	6.30	6.30	+ 5.95	10.68	8.16	1.99	0.02	0.89	+ 1.08
20—23/5	+ 450	23.72	7.63	10.30	+ 5.79	9.90	8.24	3.26	0.03	1.70	+ 1.53
26—29/5	+ 100	21.74	10.88	7.20	+ 3.66	10.22	7.73	2.99	0.02	1.93	+ 1.04
1—4/6	+ 200	18.04	8.16	6.21	+ 3.67	9.74	7.76	2.48	0.03	1.99	+ 0.46
7—10/6	+ 150	18.04	5.17	7.17	+ 5.70	7.78	7.76	2.48	0.02	2.29	+ 0.17
13—16/6	+ 200	11.62	6.73	3.22	+ 1.67	7.78	7.64	1.82	0.01	1.36	+ 0.45
19—22/6	+ 50	13.56	6.43	5.65	+ 1.46	7.78	6.54	2.12	0.01	1.89	+ 0.22
25—28/6	+ 100	15.49	6.38	7.52	+ 1.59	6.82	6.82	2.36	0.01	2.48	—0.13
1—4/7	+ 100	15.49	6.99	5.39	+ 3.11	6.32	6.54	2.36	0.04	2.47	—0.15
7—10/7	—150	14.72	6.08	5.44	+ 3.20			2.30	0.06	2.08	+ 0.16
13—16/7	+ 50	16.54	5.96	7.93	+ 2.65	5.38	5.92	2.58	0.01	2.57	+ 0.00
25—28/7						6.82					
31/7—3/8	+ 250	9.89	4.51	2.75	+ 2.63			1.32	0.01	1.35	—0.04
6—9/8	—250	13.26	6.27	4.33	+ 2.66	6.32	4.00	1.96	0.01	2.23	—0.28
12—15/8	—100	11.36	6.14	4.04	+ 1.18	6.32	3.72	7.68	0.15	6.09	+ 0.44
18—21/8	—300	9.68	5.94	4.55	—0.81	5.87	4.32	7.48	0.08	6.63	+ 0.77
24—27/8	—250	9.68	5.92	5.64	—1.88	5.87	4.49	7.48	0.05	8.22	—0.79
30/8—2/9	—500	0	3.78	0	—3.78	5.38	6.40	0	0.00	0	—0.00

⁴/₁₀ 26. (25 w.o.) W. 5250 gm. Since ²⁰/₁₀ the animal has had one or several tetanic attacks every day. Has not eaten during the past 5 days. Is in bad condition and does not want to get up.

Epiphyseal swelling is very prominent and has not decreased since commencing with the injection of the large quantities of CaCO_3 , but, on the other hand, the «Rosary» seems to have decreased a little. Killed.

Female.

P				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
3.04	0.24	1.30	+ 1.50	$\frac{4}{5}$ 26. W. 3500 gm.
3.04	0.11	1.23	+ 1.70	
3.82	0.18	2.11	+ 1.53	
3.51	0.20	1.61	+ 1.70	$\frac{20}{5}$ 26. W. 5250 gm.
2.97	0.12	1.41	+ 1.44	
2.97	0.06	1.76	+ 1.15	
2.01	0.08	0.80	+ 1.13	$\frac{13}{0}$ 26. W. 5650 gm. Slight epiphyseal swelling and «Rosary».
2.35	0.07	1.33	+ 0.95	$\frac{20}{0}$ 26. X-Rays: Broad, uneven, concave and serrated epiphyseal lines. Prominent epiphyseal swelling.
2.30	0.07	1.90	+ 0.33	
2.30	0.05	1.46	+ 0.79	$\frac{1}{7}$ 26. W. 6400 gm.
2.67	0.18	1.63	+ 0.86	
2.99	0.10	1.80	+ 0.99	$\frac{20}{7}$ 26. W. 7050 gm.
1.54	0.14	0.63	+ 0.77	$\frac{6}{8}$ 26. W. 6400 gm.
2.11	0.15	1.34	+ 0.62	$\frac{10}{8}$ 26. Considerable epiphyseal swelling and «Rosary».
				$\frac{11}{8}$ 26. 5 gm. CaCO_3 in 24 hours.
1.82	0.15	1.25	+ 0.42	$\frac{21}{8}$ 26. W. 6350 gm.
1.66	0.21	1.33	+ 0.10	$\frac{20}{8}$ 26. Yesterday the first tetanic cramp attack noted. During this period no food was taken. «Rosary» is clearly present. Large epiphyseal swelling.
1.66	0.14	1.36	+ 0.16	$\frac{2}{9}$ 26. X-Rays: Greatly increased, concave and serrated epiphyseal cartilage. Large epiphyseal swelling. Poor lime deposition.
0	0.06	0	-0.06	

Autopsy:

Lean animal, no sub-cutaneous fat.

Thorax: Small, barrel-shaped. On the inside a very prominent «Rosary». Thickening of the costo-chondral junction found on cutting through, also uneven, serrated junction.

Bones soft, even the largest epiphyses are cut through very easily. Noticeable large epiphyseal swelling. Epiphyseal cartilage broad, uneven, serrated.

Dog No. VIII.

Date	Weight bal- ance in gm.	N				Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca			
		Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.			Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1926											
8—11/5	150	14.35	3.98	4.76	+ 5.61	10.65	8.41	1.55	0.01	0.75	+ 0.79
14—17/5	450	24.61	7.50	7.03	+ 10.08	10.39	8.15	2.66	0.03	1.06	+ 1.57
20—23/5	500	29.65	12.32	5.14	+ 12.19	10.16	7.05	4.08	0.03	2.57	+ 1.48
26—29/5	850	35.58	18.54	7.30	+ 9.84		8.12	4.89	0.03	2.76	+ 2.10
1—4/6	50	28.06	8.49	17.54	+ 2.03	9.71	8.20	3.86	0.04	1.39	+ 1.43
7—10/6	100	26.06	13.33	8.96	+ 3.75	8.78	7.64	3.58	0.04	2.44	+ 1.10
13—16/6	—150	17.42	9.20	5.07	+ 3.15	7.30	6.96	2.73	0.01	2.12	+ 0.60
19—22/6	0	17.42	9.95	6.44	+ 1.03	7.30	6.68	2.73	0.02	2.10	+ 0.61
25—28/6	—400	13.55	7.70	8.29	— 2.44	7.70	6.40	2.06	0.01	1.71	+ 0.34
1—4/7	300	19.36	7.57	6.54	+ 5.25	7.22	6.40	2.95	0.04	2.33	+ 0.58
7—10/7	100	18.38	9.66	6.08	+ 2.64			2.87	0.13	2.42	+ 0.32
13—16/7	150	14.78	7.14	4.69	+ 2.90	7.30	5.62	2.30	0.04	1.44	+ 0.82
25—28/7	450	11.86	4.70	2.46	+ 4.70	6.28	3.20	1.58	0.02	1.93	— 0.37
31/7—3/8	100	21.76	9.36	5.26	+ 7.14			2.91	0.01	2.62	+ 0.28
6—9/8	—100	17.04	8.69	3.55	+ 4.80	6.82	3.67	2.51	0.03	1.42	+ 1.06
12—15/8	—500	5.67	5.41	1.89	— 1.67	6.32	3.90	0.84	0.03	1.21	— 0.60
18—21/8	—300	6.77	5.93	1.82	— 0.98	5.87	3.81	1.03	0.04	0.77	+ 0.22
24—27/8	—100	6.77	8.80	1.64	— 3.67	5.38	4.10	1.03	0.01	1.18	— 0.16
30/8—2/9	—250	7.75	5.37	2.59	— 0.22	5.78	3.64	1.18	0.01	1.33	— 0.16
5—8/9											

²/₀ 26. W. 6600 gm. X-Rays: As ¹⁰/₈ 26.

⁰/₀ 26. (26 w.o.)

During the whole period of experiment has been considered as absolutely the worst compared with No. VII and, earlier, No. IX.
Killed.

Male.

P				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
2.55	0.23	1.08	+ 1.24	⁴ / ₅ 26. W. 3700 gm.
4.20	0.15	1.63	+ 2.42	
4.93	0.30	1.77	+ 2.86	²⁰ / ₅ 26. Until to-day faeces have been almost as thin as soup.
5.87	0.32	2.28	+ 3.27	²⁰ / ₅ 26. W. 6050 gm.
4.67	0.12	1.79	+ 2.76	
4.44	0.15	1.82	+ 2.47	
3.18	0.14	1.25	+ 1.79	¹⁸ / ₆ Slight epiphyseal swelling and «Rosary».
3.18	0.17	1.54	+ 1.47	²⁰ / ₆ 26. Yesterday evening a few attacks of tetanic cramp in quick succession, particularly cramp in the muscles of the back. Attack of cramp observed for the first time a few days ago.
2.19	0.05	1.45	+ 0.69	Large epiphyseal swelling and «Rosary».
3.03	0.16	1.57	+ 1.30	X-Rays: Broad, concave, serrated epiphyseal cartilage. Prominent epiphyseal swelling.
3.49	0.28	1.57	+ 1.64	¹ / ₁ 26. W. 7350 gm.
2.84	0.27	1.25	+ 1.32	
2.01	0.28	1.18	+ 0.55	²⁸ / ₇ 26. W. 6700 gm. Light and frequent attacks of tetanic cramp.
3.50	0.19	1.61	+ 1.70	⁶ / ₈ 26. W. 7600 gm.
2.70	0.20	0.95	+ 1.55	¹⁰ / ₈ 26. Large epiphyseal swelling and «Rosary». Moves with difficulty. Marked curvature of fore-legs. X-Rays: Very great, increased, concave and serrated epiphyseal cartilage. Large epiphyseal swelling. Poor deposit of chalk. Curvature of the legs.
1.11	0.24	0.54	+ 0.33	
1.28	0.16	0.50	+ 0.62	²¹ / ₈ 26. W. 700 gm.
1.35	0.18	0.65	+ 0.52	²⁰ / ₈ 26. (24 w.o.) W. 6950 gm. Epiphyseal swelling and «Rosary» very pronounced. Has daily and, frequently, several per day, attacks of tetanic cramp, during which the animal gets nystagmus.
1.51	0.13	0.69	+ 0.69	

Result of Autopsy:

Thorax: Small, barrel-shaped. Strongly marked «Rosary» is seen on the inside, a little more so than with No. VII. The costo-chondral junction shows a swelling, is irregular serrated.

All bones soft, easily to cut through. Larger epiphyseal swelling than with No. VII.

Epiphyseal cartilage broad, irregular, serrated.

Dog No. IX.

Date	Weight bal- ance in gm.	N				Mgm. Ca in 200 c.c. serum	Mgm. P in 100 c.c. serum	Ca			
		Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.			Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1926											
8-11/5	100	12.30	4.37	3.81	+ 4.12	10.36	8.48	2.43	0.01	0.64	+ 1.78
14-17/5	250	18.46	5.36	6.00	+ 7.09	10.87	8.55	3.09	0.02	1.00	+ 2.07
20-23/5	150	17.79	6.01	6.65	+ 5.13	10.87	8.14	3.55	0.01	1.10	+ 2.44
26-29/5	150	17.79	6.86	6.42	+ 4.51		8.43	3.55	0.01	1.27	+ 2.27
1-4/6	200	20.04	7.96	7.57	+ 4.51	10.65	8.00	3.86	0.02	1.49	+ 2.35
7-10/6	50	18.04	5.82	7.25	+ 4.97	10.16	7.64	3.58	0.01	2.22	+ 1.35
13-16/6	250	19.36	7.37	5.89	+ 6.10	9.71	7.82	4.13	0.01	2.50	+ 1.62
19-22/8	50	19.36	10.28	5.39	+ 3.69	8.76	7.18	4.13	0.01	2.66	+ 1.46
25-28/6	150	21.30	14.67	8.95	- 2.42	8.76		4.35	0.02	3.20	+ 1.13
1-4/7	350	19.36	9.14	7.79	+ 2.43	8.76	6.30	4.05	0.05	3.10	+ 0.90
7-10/7	-150	16.54	8.40	6.36	+ 1.78			3.69	0.02	2.66	+ 1.01
13-16/7	300	22.05	8.49	6.32	+ 7.24	7.78	5.34	4.55	0.01	3.89	+ 0.65

Male.

P				R e m a r k s
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
2.04	0.19	0.90	+ 1.01	$\frac{4}{5}$ 26. W. 3100 gm.
3.04	0.14	1.23	+ 1.67	
2.88	0.05	1.25	+ 1.58	
2.88	0.10	1.15	+ 1.63	$\frac{29}{5}$ 26. W. 4450 gm.
3.29	0.05	1.50	+ 1.74	
2.97	0.10	1.42	+ 1.45	
3.34	0.05	1.59	+ 1.70	$\frac{13}{6}$ 26. Slight epiphyseal swelling and «Rosary».
3.34	0.06	1.71	+ 1.57	
3.14	0.06	1.92	+ 1.16	$\frac{29}{6}$ 26. X-Rays: Narrow, even epiphyseal cartilage.
2.86	0.15	1.72	+ 0.99	$\frac{1}{7}$ 26. W. 6200 gm.
2.99	0.16	1.71	+ 1.12	
3.97	0.13	2.04	+ 1.80	$\frac{25}{7}$ 26. W. 6400 gm.

$\frac{28}{7}$ 26. (20 w.o.). Found dead to-day in metabolism kennel, lying with legs outstretched as if having died during a tetanic attack. Had eaten nothing during past 3 days.

Autopsy:

No cause of death could be assigned, nothing abnormal with regard to the internal organs other than that round worm was very prevalent in the small intestine.

Thorax: Deep. A very prominent «Rosary» on the inner side, but the costo-chondral junction on being cut through, found to be almost straight and even.

The bones hard to cut through. Epiphyseal cartilage 1—1½ mm. broad, even.

Dog No. X.

Date	Weight bal- ance in gm.	N				Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca			
		Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.			Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1926											
8-11/5											
14-17/5											
20-23/5						10.72	8.18				
26-29/5	0	17.19	6.60	6.08	+ 5.11	10.68	8.41	2.45	0.05	0.90	+ 1.50
1-4/6	100	22.05	6.89	8.45	+ 6.71	10.72	8.87	3.03	0.02	1.72	+ 1.89
7-10/6	100	18.04	7.56	6.52	+ 3.96	10.68	8.42	2.48	0.03	1.10	+ 1.85
13-16/6	450	19.36	7.22	6.79	+ 5.35	10.19	8.48	3.03	0.04	0.88	+ 2.11
19-22/6	300	23.23	8.03	10.00	+ 5.20	10.19	8.00	3.64	0.01	1.54	+ 2.09
25-28/6	350	23.23	9.75	9.24	+ 4.24	10.00	7.62	3.54	0.03	1.90	+ 1.61
1-4/7	0	24.30	9.82	9.66	+ 4.72	9.71	7.80	3.69	0.07	1.35	+ 2.27
7-10/7	150	18.88	6.88	7.85	+ 3.65			2.87	0.04	1.57	+ 1.26
13-16/7	0	18.88	6.51	6.73	+ 5.14	9.71	6.96	2.87	0.04	1.72	+ 1.11
25-28/7	300	17.80	5.05	4.81	+ 7.84	10.68	6.74	2.38	0.02	1.00	+ 1.36
31/7-3/8	300	27.69	7.09	7.41	+ 14.19	10.19	7.62	3.70	0.03	2.18	+ 1.49

Female.

P				R e m a r k s
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				⁴ / ₅ 26. W. 3000 gm.
				²² / ₅ 26. No lemon juice.
2.99	0.14	1.26	+ 1.59	²⁰ / ₅ 26. W. 4600 gm.
3.62	0.13	1.60	+ 1.89	
2.97	0.21	1.22	+ 1.54	
3.34	0.18	2.40	+ 0.76	¹⁸ / ₆ 26. W. 5350 gm.
3.99	0.08	1.86	+ 2.05	²² / ₆ 26. Epiphyseal swelling slightly noticeable and incipient «Rosary».
3.48	0.18	2.09	+ 1.16	²⁰ / ₆ 26. X-Rays: Narrow, even, epiphyseal cartilage.
3.56	0.25	2.00	+ 1.31	
3.32	0.21	1.50	+ 1.61	
3.32	0.36	1.64	+ 1.32	Lemon juice 5 c.c. per diem, given from ¹⁸ / ₇ 26.
				²⁴ / ₇ 26. X-Rays: Narrow, but faint serration of the epiphyseal cartilage. Slight epiphyseal swelling and «Rosary».
2.74	0.23	1.10	+ 1.41	Cod-liver oil 10 c.c. per diem, given from ²² / ₇ 26.
4.22	0.20	1.83	+ 2.19	²⁸ / ₇ 26. W. 7100 gm.
				⁵ / ₈ 26. (21 w.o.). Been experimented upon for 11 weeks. W. 7850 gm. Epiphyseal swelling decreased, practically speaking, gone. «Rosary» disappeared altogether. Discharged from the experiment <i>alive</i> .

3rd. Series of Experiments (Nos. XI—XIV):

4 male puppies (harrier cross breed) born $\frac{0}{3}$ 27, suckled for 5 weeks, later maize-oatmeal porridge, a little milk and bread, together with one teaspoon of Cod-Liver Oil per diem, taken on $\frac{11}{7}$ 27 for experiment when 9 weeks old. Experimental diet as before.

No. XI. — 10 c.c. coconut oil.

No. XII. — 10 c.c. " " + 2 gm. calcium-lactate
(—0.367 gm. Ca) per diem.

No. XIII. — 10 c.c. coconut oil + 5 gm. salt mixture.

Dog No. XI.

Date	Weight bal- ance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P. in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Bal- ance in gm	Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1927—8											
13—16/7	+ 400	10.65	8.65	2.75	0.06	1.07	+ 1.62	3.26	0.13	1.32	+ 1.81
25—28/7	+ 900	19.24	8.88	4.88	0.02	2.24	+ 2.62	5.82	0.18	2.06	+ 2.68
6—9/8	+ 800	9.83	7.80	5.28	0.02	3.03	+ 2.23	5.61	0.33	3.98	+ 1.30
18—21/8	+ 750	9.65	7.61	5.28	0.02	1.91	+ 3.35	5.61	0.18	3.30	+ 2.13
24—27/8	+ 550	9.42	7.27	5.02	0.04	1.93	+ 3.05	5.82	0.30	4.24	+ 1.28
11—14/9	+ 600	7.37	7.27	5.33	0.04	2.88	+ 2.41	6.18	0.19	4.25	+ 1.74
23—26/9	+ 500			4.23	0.05	2.92	+ 1.26	5.58	0.17	3.72	+ 1.69
5—8/10	+ 400			3.04	0.06	1.76	+ 1.22	4.08	0.20	1.09	+ 1.79
17—20/10	+ 500			2.67	0.02	1.81	+ 0.83	4.03	0.16	1.61	+ 2.26
29—1/11	+ 350			2.67	0.04	1.83	+ 0.80	4.03	0.98	1.69	+ 1.36
10—13/11	+ 200			4.00	0.12	3.69	+ 0.19	4.44	0.55	2.91	+ 0.98
22—25/11	+ 800	8.73	5.72	4.20	0.11	2.80	+ 1.29	4.73	1.12	2.68	+ 0.93
4—7/12	+ 100			4.39	0.13	4.16	+ 0.10	5.33	0.98	3.95	+ 0.40
16—19/12	0			0.71	0.09	1.20	—0.58	1.70	0.41	1.76	—0.47
28—31/12	—150	8.42	4.28	0.55	0.04	1.66	—1.15	1.32	0.52	1.73	—0.93
9—12/1	— 50			0.57	0.04	1.02	—0.49	1.09	0.39	1.09	—0.39
21—24/1	—400	8.42	4.28	0.66	0.06	1.26	—0.66	1.27	0.39	1.37	—0.49
2—5/2	— 50	5.05	3.83	0.76	0.08	2.11	—1.43	1.45	0.48	1.62	—0.65

The salt mixture consisted of:

840 parts $\text{Ca}_3\text{P}_2\text{O}_8$

95 " CaCO_3

and 5 gm. of this mixture were given (—1.979 gm. Ca and 0.551 gm. P) per diem.

No. XIV. — 10 c.c. coconut.

The 80 % oatmeal in the experimental diet was here substituted for a corresponding amount of finely sieved *wheat flour*.

In addition all 4 received Marmite, lemon juice and CaCl_2 per diem as in the previous series of experiments.

Male.

Mg				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				¹¹ / ₇ '27. W. 4800 gm. ²⁵ / ₇ '27. W. 6250 gm. ⁰ / ₈ '27. W. 9100 gm. Incipient «Rosary», epiphyseal swelling, and bowed fore-legs. ²⁷ / ₈ '27. W. 10,500 gm. Very marked epiphyseal swelling and increasing «Rosary». ²⁸ / ₀ '27. W. 13,500 gm. ¹² / ₁₀ '27. Epiphyseal swelling and «Rosary» clearly present, not so prominent as with No. XIII. ¹ / ₁₁ '27. W. 15,150 gm. Prominent «Rosary» and epiphyseal swelling. No cramp observed. 1.55 0.04 0.78 + 0.73 ²⁵ / ₁₁ '27. (29 w.o.) W. 16,300 gm. Prominent «Rosary» and epiphyseal swelling. X-Rays: Increased, uneven epiphyseal cartilage. 1.69 0.07 1.10 + 0.52 ⁷ / ₁₂ '27. (31 w.o.) W. 16,000 gm. No cramp. Obvious, not very marked «Rosary» or epiphyseal swelling. From ⁰ / ₁₂ the diet consists of <i>oatmeal only</i> . 1.86 0.08 1.01 + 0.77 ¹² / ₁ '28. W. 14,350 gm. 1.25 0.04 0.55 + 0.70 ²⁴ / ₁ '28. W. 13,700 gm. The epiphyseal swelling has now increased considerably and the «Rosary» is very prominent. 0.98 0.04 0.50 + 0.44 ¹⁵ / ₁ '28. (41 w.o.) — 10 months. W. 13,700 gm. Killed. 0.64 0.04 0.36 + 0.24 0.75 0.03 0.44 + 0.28 0.86 0.05 0.44 + 0.37

Autopsy:

Thorax: Deep. On the inside a pronounced «Rosary». On cutting through the costo-chondral junction a comparatively straight and even junction seen between cartilage and bone.

All bones hard, the knife had to be hammered through. The epiphyseal lines narrow, even.

Dog No. XII.

Date	Weight bal- ance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.	Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1927-8											
13-16/7	+ 50	10.65	8.55	3.54	0.01	1.25	+ 2.28	2.91	0.08	1.58	+ 1.25
25-28/7	+ 450	10.24	8.65	3.76	0.02	1.90	+ 2.84	4.36	0.14	2.48	+ 1.74
6-9/8	- 300	9.42	7.80	5.06	0.02	3.45	+ 1.59	4.21	0.18	2.94	+ 1.09
18-21/8	+ 950	9.20	6.95	6.88	0.04	2.85	+ 3.99	5.61	0.17	3.20	+ 2.24
24-27/8	+ 450	9.01	6.95	4.18	0.02	2.98	+ 2.23	4.78	0.07	3.05	+ 1.61
11-14/9	+ 450	7.37	6.65	6.43	0.03	3.94	+ 2.46	6.18	0.16	4.31	+ 1.71
23-26/9	+ 550			4.53	0.08	4.74	- 0.29	4.52	0.18	3.61	+ 0.74
5-8/10	+ 650			4.16	0.02	3.30	+ 0.84	4.42	0.08	3.82	+ 0.52
17-20/10	+ 700			4.22	0.03	2.88	+ 1.81	4.71	0.13	2.08	+ 2.50
29/10-1/11	+ 400			3.33	0.06	2.11	+ 1.16	3.36	0.53	1.47	+ 1.36
10-13/11	+ 200			4.18	0.21	3.22	+ 0.75	3.42	0.84	2.22	+ 0.36
22-25/11	+ 200			5.30	0.06	3.68	+ 1.56	4.73	0.71	2.14	+ 1.88
4-7/12	0			4.32	0.15	3.71	+ 0.46	3.91	0.57	2.01	+ 1.33
16-19/12	+ 600			1.89	0.03	1.57	+ 0.29	1.89	0.16	2.69	- 0.96
28-31/12	- 150			1.65	0.02	1.63	- 0	1.52	0.12	1.90	- 0.70
9-12/1	+ 100			1.86	0.01	1.58	+ 0.27	1.45	0.15	1.97	- 0.67
21-24/1	0	6.54	5.16	1.76	0.01	1.60	+ 0.15	1.27	0.17	1.96	- 0.86
2-5/2	+ 250	6.63	6.06	2.24	0.04	3.09	- 0.80	2.18	0.21	3.22	- 1.25

¹ Obvious "Rosary", also epiphyseal swelling, fore-legs slightly bowed, also inclination to subluxation position of wrist joints.

X-Rays: Slightly increased, even epiphyseal cartilage. Slight epiphyseal swelling. Good deposit of chalk.

² No cramp. Obvious epiphyseal swelling and "Rosary", not, however, so marked as with No. XI.

From and including 9/12 27 the skimmed-milk powder excluded from diet and replaced by *oatmeal*.

Male.

Mg				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				¹¹ / ₇ 27. W. 4000 gm.
				²⁵ / ₇ 27. W. 5550 gm.
				⁹ / ₈ 27. W. 6350 gm. Bones normal.
				²⁷ / ₈ 27. W. 7550 gm. Inclination towards epiphyseal swelling and «Rosary».
				²⁶ / ₉ 27. W. 10,350 gm.
				¹² / ₁₀ 27. Neither epiphyseal swelling, nor «Rosary» now present.
				¹ / ₁₁ 27. W. 12,500 gm. «Rosary» and epiphyseal swelling present. No cramp.
1.20	0.04	0.99	+ 0.17	
1.70	0.02	1.24	+ 0.44	²⁵ / ₁₁ 27. W. 13,200 gm. ¹
1.86	0.06	0.69	+ 0.61	⁷ / ₁₂ 27. (31 w.o.) W. 13,000 gm. ²
1.39	0.02	0.63	+ 0.74	
0.98	0.01	0.55	+ 0.42	
0.85	0.01	0.65	+ 0.19	¹² / ₁ 28. W. 12,200 gm.
0.75	0.01	0.60	+ 0.14	²⁴ / ₁ 28. W. 11,950 gm. Epiphyseal swelling just visible, but can be felt. «Rosary» very faintly evident.
1.28	0.02	0.67	+ 0.59	¹⁴ / ₂ 28. (841 w.o.) — 10 months. W. 12,300 gm. Slight epiphyseal swelling, palpable «Rosary». Killed.

Result of Autopsy:

Thorax: Deep; on the inside very pronounced «Rosary», but less than with No. XI. Costo-chondral junction almost straight, slightly swollen. All bones comparatively hard. The knife had to be hammered through the large bones.

Epiphyseal cartilage slightly broad and uneven.

Dog No. XIII.

Date	Weight balance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Balance in gm.	Total intake	gm. in urine	gm. in faeces	Balance in gm.
1927-8											
13-16/7	+ 350	10.24	8.00	8.68	0.06	4.58	+ 4.04	4.91	0.16	2.15	+ 2.60
25-28/7	+ 450	10.24	8.42	9.60	0.07	5.67	+ 3.86	6.01	0.17	3.47	+ 2.37
6-9/8	0	9.42	7.61	9.90	0.11	6.13	+ 3.66	5.86	0.30	4.42	+ 1.14
18-21/8	+ 50	9.29	7.27	7.92	0.01	6.00	+ 1.91	3.75	0.06	2.68	+ 1.01
24-27/8	+ 450	9.42	6.66	10.01	0.13	5.96	+ 3.92	6.37	0.08	3.32	+ 2.97
11-14/9	+ 250	8.60	8.40	11.27	0.15	8.46	+ 2.66	7.83	0.22	5.10	+ 2.51
23-26/9	+ 500			10.16	0.19	8.09	+ 1.88	7.22	0.18	4.00	+ 3.04
5-8/10	+ 600			9.44	0.13	8.42	+ 0.89	6.74	0.19	4.15	+ 2.40
17-20/10	+ 600			9.28	0.14	8.33	+ 0.81	6.69	0.17	2.21	+ 4.31
²⁶ / ₁₀ - ¹ / ₁₁	+ 500			9.28	0.24	7.51	+ 1.53	6.69	0.82	3.36	+ 2.51
10-13/11	0			9.02	0.84	6.48	+ 1.70	5.07	0.69	1.96	+ 2.42
22-25/11	+ 500	8.60	8.42	10.46	0.13	6.17	+ 4.26	6.74	0.65	2.17	+ 3.92
4-7/12	+ 100			10.32	0.07	9.02	+ 1.23	6.98	0.42	4.31	+ 2.25
16-19/12	+ 250			7.12	0.13	6.31	+ 0.68	4.48	0.32	3.59	+ 0.57
28-31/12	- 450	8.73	5.52	6.88	0.05	7.12	- 0.29	3.91	0.41	2.99	+ 0.51
9-12/1	- 300			6.88	0.04	7.26	- 0.42	3.47	0.37	2.13	+ 0.97
21-24/1	0	7.92	3.88	6.88	0.04	7.97	- 1.13	3.47	0.33	2.47	+ 0.67
2-5/2	+ 400	6.08	4.21	7.26	0.04	5.82	+ 1.40	4.20	0.27	2.12	+ 1.81
14-17/2	- 400			6.60	0.04	5.92	+ 0.64	2.92	0.23	1.85	+ 0.84

¹ «Rosary» and epiphyseal swelling very prominent. Fore-legs bowed, inclination to subluxation position of wrist joints. Stiffness in whole of body, walking also appears affected by rigidity. No cramp observed but excess-irritability present.

² Prominent epiphyseal swelling, more so than with No. XI and XII, subluxation position of the wrist joints. Fore-legs very bowed. «Rosary» not so prominent. Large and lively. X-Rays: Decreased, even epiphyseal cartilage. Obvious epiphyseal swelling. Good deposit of chalk.

³ Prominent epiphyseal swelling; fore-legs bowed, also «Rosary». No cramp. From and including ⁹/₁₂ 27 the skimmed-milk powder deleted from diet and replaced by *oatmeal*.

Male.

Mg				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				¹¹ / ₇ 27. W. 4250 gm. ²⁰ / ₇ 27. W. 5700 gm. ⁹ / ₈ 27. W. 7550 gm. Bones normal. ²⁷ / ₈ 27. W. 8450 gm. Obvious epiphyseal swelling and incipient curvature of fore-legs. Slight «Rosary». ²⁰ / ₉ 27. W. 11,400 gm. ¹³ / ₁₀ 27. Prominent epiphyseal swelling. Very prominent «Rosary». ¹ / ₁₁ 27. (25 w.o.) w. 14,400 gm. ¹ 1.20 0.01 0.72 + 0.47 1.83 0.03 1.51 + 0.29 ²⁵ / ₁₁ 27. (29 w.o.) w. 14,800 gm. ² 1.86 0.04 1.16 + 0.66 ⁷ / ₁₂ 27. (31 w.o.) w. 14,300 gm. ³ 2.09 0.02 1.36 + 0.71 1.67 0.01 0.79 + 0.88 1.07 0.03 0.64 + 0.40 ¹³ / ₁ 28. W. 15,000 gm. 1.07 0.01 0.59 + 0.47 ²⁴ / ₁ 28. W. 15,000 gm. Epiphyseal swelling and «Rosary» about as before. 1.50 0.01 0.60 + 0.89 0.75 0.02 0.55 + 0.18 ¹⁸ / ₂ 28. (40 w.o.) — 10 months. w. 14,400 gm. ⁴

⁴ Obvious «Rosary» and epiphyseal swelling, fore-legs bowed. Large dog, appears to be somewhat leaner than No. XII.

Killed.

Result of Autopsy:

Quite a large swelling of the costo-chondral junctions («Rosary») on the inside of thorax, but not so prominent as with No. XII. On cutting through, junctions found to be almost even.

All bones hard. Epiphyseal cartilage quite narrow, a little irregular.

Dog No. XIV.

Date	Weight bal- ance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.	Total in gm.	gm. in urine	gm. in faeces	Bal- ance in gm.
1927-28											
13-16/7	+ 550	10.65	8.65	2.56	0.28	0.26	+ 2.02	3.72	0.43	0.38	+ 2.91
25-28/7	+ 850	10.65	8.88	4.60	0.08	0.48	+ 4.04	4.78	0.29	0.68	+ 3.81
6-9/8	- 50	9.83	7.80	2.48	0.03	0.27	+ 2.18	2.50	0.19	0.66	+ 1.65

Male.

R e m a r k s

¹¹/₇ 27. W. 4800 gm. *Wheat flour* instead of oatmeal.

²⁵/₇ 27. W. 6400 gm.

⁹/₈ 27. (13 w.o.) W. 8100 gm.

Bones normal.

¹⁸/₈ 27. W. 9000 gm.

Acute gastro-enteritis.

²¹/₈ 27. To-day, cramp in hind-legs. Cannot walk.

²²/₈ 27. Still ill. Killed.

Result of Autopsy:

Bones normal.

4th Series of Experiments.

3 male dogs, Nos. XV—XVIII, born $^{30}/_{8}$ 1927. Dam: grey deer-hound;
sire: German sheep dog (schäfer).

The puppies were suckled until $^{17}/_{6}$ 27, for four weeks; received maize
and oatmeal porridge, milk and bread and were put on a rickets-producing
diet $^{24}/_{6}$ 27 when 5 weeks old.

No. XV was given milk powder (20 %); oatmeal (80 %)

" XVI " " " " (20 %); wheat flour (80 %)

" XVII " " " " " oatmeal only.

Dog No. XV.

Date	Weight bal- ance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.	Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1927											
29/9—2/10	+ 50			0.79	0.02	0.55	+ 0.22	1.04	0.05	0.42	+ 0.57
11—14/10	+ 250			1.11	0.01	0.92	+ 0.18	1.68	0.06	0.73	+ 0.89
23—26/10	+ 350			1.33	0.01	1.12	+ 0.20	2.02	0.06	0.83	+ 1.13
4—7/11	+ 250	8.73	5.33	1.85	0.01	1.32	+ 0.52	2.05	0.14	0.91	+ 1.00
16—19/11	+ 350	8.24	5.04	1.93	0.01	1.44	+ 0.48	2.18	0.10	1.44	+ 0.84
$^{28}/_{11}$ — $^{1}/_{12}$	+ 50			1.61	0.03	0.01	+ 0.57	1.82	0.18	0.82	+ 0.82
10—13/12	+ 200	8.73	4.93	1.46	0.01	1.21	+ 0.24	1.78	0.03	0.62	+ 1.13

¹ Is better than Nos. XVI and XVII; appears fat by comparison. Jumps
lively around. The epiphyseal swelling on the fore-legs has become so
marked that an inclination to subluxation position of wrist joints appears.
Bowed legs, convex. Considerable epiphyseal swelling on the hind-legs as
well. Very prominent «Rosary» but not so marked as with Nos. XVI
or XVII.

$^{12}/_{12}$ 27. Killed.

Result of Autopsy:

Some sub-cutaneous fat.

Thorax: Very prominent «Rosary» on the inside.

In addition each received per diem:

10 c.c. coconut oil (hardened)
 5 " lemon juice
 5 gm. marmite
 1.5 " NaCl.

No. XVIII, brother of Nos. XV—XVII was given throughout ordinary dog's food consisting of maize and oatmeal porridge, bread, meat and meat bones, skimmed and unskimmed milk as well as about 15 c.c. cod-liver oil per diem. It was not submitted to experiment but was killed as a control animal for the other three.

Male.

Mg				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				²⁴ / ₁₀ 27. W. 1800 gm. ²⁷ / ₁₀ 27. W. 1750 gm. ¹⁴ / ₁₀ 27. W. 2450 gm.
0.72	0.01	0.25	+ 0.46	²⁸ / ₁₀ 27. Obvious epiphyseal swelling and «Rosary» present. ⁴ / ₁₁ 27. (11 w.o.) W. 3650 gm. Has been on the diet for 6 weeks. Prominent «Rosary» and very marked epiphyseal swelling. Also, bowed front legs. Obvious swelling of the distal tibia epiphyses. No cramp.
0.84	0.01	0.46	+ 0.37	¹⁰ / ₁₁ 27. W. 3850 gm.
0.65	0.01	0.27	+ 0.37	²² / ₁₁ 27. X-Rays: Greatly increased, concave and serrated epiphyseal cartilage. Prominent epiphyseal swelling and very bowed legs. Bad deposit of chalk.
0.62	0.01	0.16	+ 0.45	⁷ / ₁₂ 27. (16 w.o.) W. 4100 gm. ¹² / ₁₂ 27. (17 w.o.) Epiphyseal swelling and «Rosary» both increasing. Comparatively lively, jumps about playfully. ¹

Costa: on being cut through showed an uneven and partly serrated costo-chondral junction.

Femur. Epiphyseal cartilage broad, uneven, serrated, both the proximal and distal.

Tibia: the proximal epiphyseal cartilage 3—4 mm. broad, very uneven and serrated.

Humerus: as tibia.

Radius: the distal epiphyseal cartilage from 2—4 mm. broad, uneven, serrated.

Ulna: The distal epiphyseal cartilage about 5—6 mm. broad, uneven.

All bones soft and could be easily cut through with a small knife.

Dog No. XVI.

Date	Weight balance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Balance in gm.	Total intake	gm. in urine	gm. in faeces	Balance in gm.
1927											
²⁰ / ₀ — ² / ₁₀	+ 300			1.07	0.03	0.18	+ 0.86	0.83	0.07	0.27	+ 0.49
11—14/10	+ 300			1.80	0.03	0.23	+ 1.54	1.34	0.09	0.49	+ 0.76
23—26/10	+ 300			1.80	0.01	0.35	+ 1.44	1.34	0.06	0.42	+ 0.86
4—7/11	+ 500	9.21	4.34	2.16	0.04	0.80	+ 1.32	1.66	0.16	0.40	+ 1.10
16—19/11	+ 450	7.27	4.24	2.16	0.06	1.22	+ 0.88	1.66	0.16	0.63	+ 0.87
²⁸ / ₁₁ — ¹ / ₁₂	— 150			1.08	0.03	0.31	+ 0.74	0.83	0.10	0.16	+ 0.57
10—13/12	— 100	5.30	3.07	0.90	0.04	0.21	+ 0.65	0.67	0.08	0.05	+ 0.54

¹ During the past 4 weeks tetanic cramp attacks have been observed practically every day, sometimes several times daily. Moreover, the animal has given the impression that it has completely lost its sense of equilibrium, it reels when it walks, even when standing still, and holds its head slantwise (to the right ear). Inclination to craniotabes. The large fontanel seems to be open. Exophthalmus, not, however, very prominent.

Very marked "Rosary", more pronounced than in Nos. XV and XVII.

Considerable epiphyseal swelling, and bowed fore-legs very marked. Epiphyseal swelling also marked on hind-legs. Lean. Quite lively.

¹⁵/₆ 27. Killed.

Male.

Mg				R e m a r k s
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				²⁴ / ₉ 27. W. 1800 gm.
				² / ₁₀ 27. W. 2050 gm.
				¹⁴ / ₁₀ 27. W. 2600 gm.
				²² / ₁₀ 27. Epiphyseal swelling and «Rosary» clearly present.
0.19	0.01	0.12	+0.06	⁴ / ₁₁ 27. (11 w.o.) W. 3600 gm. Both epiphyseal swelling and «Rosary» have increased to a very considerable degree and are thus more marked than with No. XIV. Fore-legs very bowed. Also very clear epiphyseal swelling of the distal tibia epiphyses. No cramp observed.
0.19	0.02	0.23	—0.06	¹⁹ / ₁₁ 27. W. 4600 gm.
0.10	0.01	0.03	+0.06	²³ / ₁₁ 27. <i>X-Rays</i> : Exceptionally broad, concave and serrated epiphyseal cartilage, more so than in No. XV. Epiphyseal swelling considerable, bowed legs pronounced. Deposit of chalk seems better than with No. XV.
0.14	0.01	0.02	+0.11	⁷ / ₁₂ 27. (16 w.o.) Attacks of cramp have been observed almost daily for the past 14 days but they soon pass over. The head is held constantly to the right side. Considerable epiphyseal swelling and «Rosary» greater than with No. XV. Lean.
				¹⁵ / ₁₂ 27. (17 w.o.) W. 4100 gm. ¹

Result of Autopsy:

Lean. No sub-cutaneous fat.

Thorax: Showed more marked «Rosary» than No. XVII. The rib clearly much harder to cut through than in case of No. XVII.

Femur: Epiphyseal cartilage 2—3 mm. broad, uneven, serrated, worse than No. XVII.

Tibia: The proximal epiphyseal cartilage 3—5 mm. broad, very uneven and serrated.

Humerus; radius and ulna: Epiphyseal cartilage broad, uneven and serrated.

All bones could be cut through easily; not, however, so soft as in No. XVII.

Date	Weight bal- ance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.	Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1927											
20/9—2/10	— 0			0.20	0.02	0.70	—0.52	0.57	0.05	0.52	—0.00
11—14/10	— 40			0.26	0.00	0.66	—0.40	0.76	0.00	0.59	+0.17
23—26/10	+250			0.33	0.01	0.80	—0.48	0.95	0.05	0.73	+0.17
4—7/11	+100	8.73	4.04	0.26	0.06	0.71	—0.51	0.76	0.06	0.62	+0.08
16—19/11	+ 20	6.79	5.04	0.24	0.02	0.64	—0.42	0.57	0.13	0.70	—0.26
28/11—1/12	÷ 60			0.12	0.01	0.29	—0.18	0.28	0.07	0.30	—0.09
10—13/12	—130	6.93	3.58	0.08	0.01	0.28	—0.21	0.19	0.02	0.18	—0.01

Result of Autopsy:

Practically speaking no sub-cutaneous fat present.

Thorax: Small. Both on the outside and especially on the inside an exceptionally pronounced «Rosary».

Costa: Soft, could quite easily be cut through. Uneven, serrated costo-chondral junction.

Right Femur: Showed an old fracture, just above the condyles, in the

Male.

Mg				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				²⁴ / ₉ 27. W. 2100 gm.
				² / ₁₀ 27. W. 1850 gm.
				¹⁴ / ₁₀ 27. W. 2060 gm.
				²⁸ / ₁₀ 27. Very pronounced "Rosary" and epiphyseal swelling.
0.54	0.01	0.28	+ 0.25	⁶ / ₁₁ 27. (11 w.o.) W. 2900 gm. "Rosary" and epiphyseal swelling increased considerably and now more marked than with No. XV. Curvature of the fore-legs with the wrist joints in a position resembling subluxation. No cramp.
0.42	0.01	0.41	- 0.00	¹⁶ / ₁₁ 27. W. 3020 gm.
0.21	0.01	0.10	+ 0.10	²⁸ / ₁₁ 27. X-Rays: A bad photograph owing to defective lime deposition. Exceptionally broad, concave, serrated epiphyseal cartilage. Large epiphyseal swelling. Curvature of the legs.
0.14	0.01	0.05	+ 0.08	⁷ / ₁₂ 27. (16 w.o.) During the past 14 days practically speaking has been quite still, does not get up or walk around. Large epiphyseal swelling and "Rosary". No cramp. Eats little, 50 gm. diet per diem only.
				¹⁵ / ₁₂ 27. (17 w.o.) W. 2320 gm. Has lain quietly in its kennel during the past 4 weeks. When lifted it appears as if the distal radius and ulna epiphyses are not really bone, and that there is complete luxation of the wrist joints. Legs very bowed. Large epiphyseal swelling on the hind-legs as well. Very pronounced "Rosary". Craniotabes. The large fontanel open. No cramp. Killed.

process of healing. The proximal epiphyseal cartilage was narrow and even, as also that in the *humerus*, while the proximal epiphyseal cartilage in the tibia was broad, uneven, likewise the epiphyseal cartilage in the *radius* and *tibia*.

All bones were exceptionally soft. The shaft of the femur was almost as thin as paper.

Dog No.

A normal male dog, brother of No. XV—VII. Diet consisting of: Maize-oatmeal porridge, skimmed milk, bread, meat and fish-bone + cod-liver oil.

¹⁵/₁₂ 27. Large, fat, lively. Weight 10,200 gm.

No sign of rickets.

Ca 10.60 }
P 8.84 } mgm. in 100 c.c. serum.

¹⁹/₁₂ 27. Killed.

5th Series of Experiments.

The group consisted of three puppies designated in the Register of Experiments as Nos. XIX, XX, XXI. They were born on ⁸/₂ 1929 and taken for experiment on ²⁴/₃ 29 (6 weeks old).

The diet for all three consisted of:

Oatmeal 80 %

Meat 20 %

Dog No. XIX.

Date	Weight bal- ance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.	Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1929											
24—27/3				0.16	0.01	0.18	—0.05	0.33	0.06	0.40	—0.13
6—9/4	+ 100			0.40	0.01	0.44	—0.05	0.99	0.08	1.24	—0.33
19—22/4	+ 150	12.8	8.33	0.50	0.01	0.42	+ 0.07	1.23	0.04	1.70	—0.51
2—5/5	+ 50			0.29	0.01	0.22	+ 0.06	0.70	0.05	0.68	—0.03
15—18/5	—250	7.6	2.2	0.17	0.01	0.15	+ 0.01	0.41	0.05	0.44	— 0.08
28—31/5	+ 200			0.20	0.01	0.22	—0.03	0.49	0.07	0.44	—0.02
10—13/6	+ 150	5.5	4.6	0.10	0.01	0.22	—0.13	0.25	0.06	0.33	—0.14

XVIII.

Result of Autopsy:

An exceptionally great layer of fat everywhere, also on viscera.

Thorax: Large, well-built. On the inside, the junction between cartilage and rib-bone was seen protruding slightly, with the junction sharp and straight.

Costa: when cut through showed a straight, sharp boundary between cartilage and bone.

All epiphyseal cartilage narrow, 1—2 mm. broad, even, without serration. The bones very hard.

In addition each received 10 c.c. coconut oil, 5 gm. marmite and 1.5 gm. NaCl per diem.

No. XIX received an extra portion of some Ca or P salt, No. XX received 2 gm. calcium lactate per diem and No. XXI received 3 gm. $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ per diem.

Male.

Total intake	Mg			Remarks
	gm. in urine	gm. in faeces	Balance in gm.	
				¹¹ / ₃ 29. W. 1950 gm.
0.25	0.01	0.10	+ 0.14	²⁴ / ₃ 29. W. 2300 gm. Taken for experiment.
0.73	0.01	0.40	+ 0.32	¹⁰ / ₄ 29. Obvious «Rosary», and epiphyseal swelling on fore legs.
0.92	0.01	0.41	+ 0.50	¹⁰ / ₄ 29. W. 4000 gm.
0.52	0.01	0.17	+ 0.34	⁷ / ₅ 29. W. 4450 gm.
				⁹ / ₅ 29. Is a little stiff in the hind legs.
0.31	0.01	0.08	+ 0.22	¹⁰ / ₅ 29. Stiff hind legs. Will not walk.
0.36	0.01	0.07	+ 0.28	² / ₆ 29. Bad. Cannot stand.
				³ / ₆ 29. The animal had cramp in the legs.
0.18	0.01	0.08	+ 0.09	¹⁰ / ₆ 29. Several attacks of cramp daily.
				²⁰ / ₆ 29. W. 3150 gm. Killed. Autopsy: Marked «Rosary». Femur soft. Epiphyseal cartilage broad, uneven.

Dog No. XX.

Date	Weight bal- ance in gm.	Mgm. Ca in 100 c.c. serum	Mgm. P in 100 c.c. serum	Ca				P			
				Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.	Total intake	gm. in urine	gm. in faeces	Bal- ance in gm.
1929											
24—27/3				0.65	0.01	0.09	+ 0.55	0.83	0.14	0.15	+ 0.04
6—9/4	— 50			0.72	0.01	0.25	+ 0.46	0.49	0.06	0.61	— 0.18
19—22/4	+ 250	12.8	8.69	1.39	0.01	0.66	+ 0.72	1.47	0.05	2.27	— 0.85
2—5/5	+ 50			1.18	0.01	0.38	+ 0.79	0.99	0.09	0.88	+ 0.02
15—18/5	— 50	6.8	4.6	1.15	0.02	0.44	+ 0.69	0.90	0.15	0.74	+ 0.01
28—31/5	— 0			1.18	0.02	0.71	+ 0.45	0.99	0.14	1.16	— 0.31
10—13/6	+ 100	6.2	6.6	1.16	0.01	0.71	+ 0.44	0.97	0.16	1.18	— 0.37

Dog No. XXI.

1929											
24—27/3				0.13	0.02	0.15	— 0.04	1.36	0.11	0.38	+ 0.87
6—9/4	+ 150			0.40	0.01	0.51	— 0.12	2.55	0.10	1.96	+ 0.49
19—22/4	— 100	9.95	5.13	0.39	0.01	0.35	+ 0.03	2.51	0.03	1.33	+ 1.15
2—5/5	— 100			0.20	0.01	0.20	— 0.01	2.05	0.05	1.06	+ 0.94
15—18/5	÷ 50	7.30	5.40	0.18	0.01	0.21	— 0.04	2.02	0.05	0.85	+ 1.12
28—31/5	— 200			0.19	0.01	0.25	— 0.07	2.03	0.03	0.94	+ 1.06
10—13/6	— 0	5.00	7.40	0.20	0.02	0.23	— 0.05	2.05	0.13	0.80	+ 1.12

Male.

Mg				Remarks
Total intake	gm. in urine	gm. in faeces	Balance in gm.	
				¹¹ / ₃ 29. W. 2090 gm.
0.25	0.01	0.05	+ 0.19	²⁴ / ₃ 29. W. 2600 gm. Taken for experiment.
0.87	0.01	0.20	+ 0.16	¹⁰ / ₄ 29. Obvious «Rosary», also epiphyseal swelling on fore-legs.
1.09	0.01	0.60	+ 0.48	¹⁹ / ₄ 29. W. 3900 gm.
0.73	0.01	0.24	+ 0.48	²⁵ / ₄ 29. Legs obviously bowed.
				² / ₅ 29. W. 4750 gm.
0.67	0.01	0.19	+ 0.47	¹⁹ / ₅ 29. Cannot walk so well as No. XXI.
0.73	0.02	0.25	+ 0.46	
0.71	0.04	0.26	+ 0.41	¹⁰ / ₆ 29. W. 5700 gm.
				²⁵ / ₆ 29. W. 5800 gm. Killed. Autopsy: «Rosary» most marked on the inside. The costo-chondral junction is uneven, swollen. Bones harder than in case No. XIX. Epiphyseal cartilage broader and more irregular.

Male.

				¹¹ / ₃ 29. W. 2150 gm.
0.25	0.02	0.10	+ 0.13	²⁴ / ₃ 29. W. 2500 gm. Taken for experiment.
0.73	0.01	0.46	+ 0.26	¹⁰ / ₄ 29. Obvious «Rosary» and epiphyseal swelling on fore-legs.
0.71	0.01	0.28	+ 0.42	¹⁹ / ₄ 29. W. 3950 gm.
				³⁰ / ₄ 29. Will not walk.
0.36	0.02	0.15	+ 0.19	⁶ / ₅ 29. Is somewhat stiff in the hind-legs, worse than No. XX at walking.
0.34	0.01	0.11	+ 0.22	¹⁵ / ₅ 29. W. 3800 gm.
0.35	0.01	0.12	+ 0.22	²⁸ / ₅ 29. W. 4000 gm.
0.36	0.04	0.25	+ 0.07	¹⁰ / ₆ 29. W. 3750 gm.
				²⁶ / ₆ 29. W. 3350 gm. Killed. Autopsy: «Rosary» most marked on the inside. The costo-chondral junction uneven, swollen. Bones harder than is the case with No. XIX (like No. XX). Epiphyseal cartilage broader and more irregular than No. XX.

Bone Analyses:

Dog No.	Bone	% Water & Fat	% Ash in	
			Fresh wgt.	Dry wgt.
I. Oatmeal Skimmed Milk powder 10 c.c. coconut oil	Femur	80.11	8.44	42.05
	Humerus	73.47	9.35	34.78
	Radius	84.92	9.02	33.24
	Ulna	79.02	11.36	54.21
II. Oatmeal Skimmed Milk powder 10 c.c. cod-liver oil	Femur	68.19	17.60	55.34
	Femur-shaft	63.37	21.62	59.06
	Humerus	68.03	18.55	54.80
	Radius	58.92	22.53	54.56
	Ulna	58.59	22.53	54.56
III. As for No. II	Femur	61.16	21.86	56.39
	Femur-shaft	58.65	25.33	61.30
	Humerus	60.89	21.73	55.55
	Radius	55.90	24.17	54.66
	Ulna	56.40	25.46	58.38
IV. Oatmeal Skimmed Milk powder 10 c.c. coconut oil Later: 10 c.c. cod-liver oil	Femur	69.50	16.17	53.23
	Femur-shaft	65.30	20.55	59.21
	Humerus	63.43	19.69	54.39
	Radius	62.50	20.32	54.20
	Ulna	57.45	22.68	53.30
V. As for No. I	Femur	81.17	7.10	37.73
	Femur-shaft	—	—	45.94
	Humerus	80.71	8.13	38.47
	Radius	76.05	8.59	35.67
	Ulna	75.39	9.40	37.48

1st. Series of Experiments.

% Ca in			% P in		
Fresh wgt.	Dry wgt.	Ash	Fresh wgt.	Dry wgt.	Ash
2.85	14.22	33.75	1.89	6.96	16.52
2.88	11.69	30.66	1.71	6.37	18.31
3.46	12.75	38.34	1.59	5.85	17.60
4.48	21.36	39.41	1.93	9.19	16.96
6.79	21.87	38.58	3.04	9.54	17.24
7.17	19.59	33.36	3.58	9.77	16.54
6.93	20.48	37.41	3.18	9.40	17.16
8.60	20.92	38.15	3.85	9.37	17.09
7.62	18.39	33.83	3.91	9.43	17.35
8.21	21.14	37.57	4.03	10.29	18.45
9.24	22.37	36.50	4.95	11.98	19.54
7.82	20.00	35.99	4.15	10.61	19.09
9.02	20.40	37.34	4.56	10.30	18.85
9.57	21.96	37.61	4.67	10.73	18.33
5.82	19.14	35.96	2.69	8.64	16.24
7.50	21.61	36.61	3.80	10.94	18.48
7.27	19.87	36.54	3.31	9.05	16.64
7.38	19.67	36.29	3.43	9.13	16.86
8.62	20.27	38.03	3.84	9.02	16.91
2.32	12.31	32.62	1.87	7.30	19.34
—	15.95	34.72	—	8.73	19.00
2.68	12.80	33.00	1.58	7.48	19.42
2.85	11.84	33.29	1.80	7.45	20.89
3.78	16.12	40.34	1.92	7.69	20.52

Bone Analyses:

Dog No.	Bone	% Water & Fat	% Ash in	
			Fresh wgt.	Dry wgt.
VI. Oatmeal Skimmed Milk powder 10 c.c. cod-liver oil 5 c.c. lemon juice	Femur	52.76	27.74	58.72
	Femur shaft	45.76	33.99	62.52
	Tibia	49.94	28.58	57.11
	Humerus	54.12	25.45	55.46
	Radius	49.07	30.10	59.12
	Ulna	48.99	29.98	59.17
VII. Oatmeal Skimmed Milk powder 10 c.c. coconut oil 5 c.c. lemon juice	Femur	70.00	13.80	46.02
	Femur-shaft	62.15	21.75	57.50
	Humerus	67.75	15.35	42.42
	Radius	63.19	15.70	42.65
	Ulna	62.82	17.60	47.31
VIII. Oatmeal Skimmed Milk powder 10 c.c. coconut oil 2 gm. Na_2HPO_4 5 c.c. lemon juice	Femur	71.06	13.26	45.85
	Femur-shaft	62.61	21.75	58.16
	Tibia	66.82	14.24	42.95
	Humerus	69.28	13.81	43.34
	Radius	66.30	14.77	43.23
	Ulna	63.40	16.19	44.25
IX. Oatmeal Skimmed Milk powder 10 c.c. coconut oil 2 gm. calcium lactate 5 c.c. lemon juice	Femur	66.71	16.28	48.90
	Tibia	65.80	17.83	50.69

2nd. Series of Experiments.

% Ca in			% P in			% Mg. in		
Fresh wgt.	Dry wgt.	Ash	Fresh wgt.	Dry wgt.	Ash	Fresh wgt.	Dry wgt.	Ash
11.27	21.42	36.49	5.24	11.09	18.89			
13.15	24.23	34.53	6.62	12.19	19.50			
10.28	20.52	35.96	5.53	11.05	19.36			
9.75	21.26	38.32	4.47	9.75	17.58	0.19	0.41	0.74
11.23	22.05	37.30	4.97	9.75	16.50	0.23	0.44	0.75
11.30	22.26	37.54	4.93	9.69	16.38	0.21	0.42	0.71
5.43	18.08	39.31	2.66	8.85	19.24			
7.78	20.56	35.76	4.25	11.22	19.52			
5.08	15.76	37.15	2.47	7.67	18.07	0.12	0.39	0.91
5.80	15.76	36.96	2.82	7.67	17.98	0.14	0.39	0.90
6.44	17.32	36.62	3.13	8.41	17.77	0.16	0.43	0.91
4.90	16.93	36.95	2.56	8.45	19.32			
7.52	21.05	36.21	4.11	11.00	18.95			
5.37	16.18	37.97	2.56	7.71	17.94			
4.98	16.21	37.40	2.44	7.94	18.32	0.10	0.31	0.73
5.31	15.75	36.44	2.58	7.67	17.72	0.12	0.34	0.79
6.06	16.55	37.41	2.91	7.96	17.99	0.14	0.37	0.83
7.20	18.63	38.11	3.04	9.14	18.68			
6.48	18.96	37.41	3.37	9.86	19.45			

Bone Analyses:

Dog No.	Bone	% Water & Fat	% Ash in	
			Fresh wgt.	Dry wgt.
XI. Oatmeal Skimmed Milk powder 10 c.c. coconut oil	Femur	67.72	18.41	54.46
	Femur-shaft	61.13	24.28	62.59
	Tibia	60.39	18.86	47.58
	Humerus	62.77	16.38	44.01
	Radius	59.23	20.31	49.82
XII. Oatmeal Skimmed Milk powder 2 gm. calcium lactate	Femur	61.81	20.56	53.85
	Femur-shaft	60.12	24.47	61.60
	Tibia	55.51	23.30	52.52
	Humerus	61.42	19.24	49.87
	Radius	65.63	17.20	50.06
	Ulna	55.03	23.57	52.42
XIII. Oatmeal Skimmed Milk powder 10 c.c. coconut oil 5 gm. Salt mixture (Ca ₃ .P ₂ .C ₈ +CaCO ₃)	Femur	60.52	22.22	56.46
	Femur-shaft	57.50	26.59	62.38
	Tibia	54.42	24.79	54.39
	Humerus	58.65	22.00	53.18
	Radius	50.27	27.56	55.22
	Ulna	46.22	28.56	53.09
XIV. Wheat-flour Skimmed Milk powder 10 c.c. coconut oil	Femur	68.00	16.55	51.72
	Femur-shaft	61.77	21.38	55.95

3rd. Series of Experiments.

% Ca in			% P in			% Mg. in		
Fresh wgt.	Dry wgt.	Ash	Fresh wgt.	Dry wgt.	Ash	Fresh wgt.	Dry wgt.	Ash
6.70	19.82	36.39	3.00	8.86	16.27	0.12	0.54	0.63
9.06	23.31	37.24	3.45	8.89	14.16	0.16	0.42	0.68
7.17	18.10	38.04	3.19	8.05	16.91	0.14	0.35	0.74
6.58	17.56	39.89	2.83	7.60	17.27	0.12	0.33	0.74
7.71	18.91	37.96	3.35	8.21	16.47	0.13	0.39	0.79
7.17	18.72	34.89	3.90	8.92	16.57	0.14	0.37	0.69
9.04	22.69	36.93	3.54	8.89	14.47	0.19	0.49	0.79
8.74	19.65	37.42	3.86	8.67	16.51	0.20	0.45	0.86
7.17	18.59	37.27	3.26	8.46	16.96	0.17	0.45	0.89
6.43	18.71	37.37	2.99	8.71	17.40	0.14	0.39	0.78
8.99	20.00	38.15	3.84	8.55	16.31	0.20	0.45	0.85
8.06	20.43	36.20	3.53	7.12	15.88	0.14	0.36	0.64
10.03	23.61	37.85	3.82	8.98	14.40	0.18	0.41	0.66
9.17	20.12	37.00	3.89	8.54	15.82	0.18	0.39	0.71
8.14	19.69	37.03	3.48	8.42	15.82	0.15	0.37	0.69
10.32	20.76	37.60	4.44	8.93	16.17	0.19	0.38	0.69
10.75	19.97	37.62	4.69	8.72	16.43	0.20	0.37	0.69
6.39	19.98	38.64	2.89	0.03	17.43	0.11	0.34	0.65
8.16	21.34	38.14	3.60	9.41	16.82	0.13	0.34	0.62

Bone Analyses:

Dog No.	Bone	% Water & Fat	% Ash in	
			Fresh wgt.	Dry wgt.
XV. Oatmeal Skimmed Milk powder 10 c.c. coconut oil	Femur	75.28	10.40	42.08
	Femur-shaft	70.13	15.78	52.25
	Tibia	72.97	10.24	37.90
	Humerus	73.69	10.62	40.35
	Radius	72.09	10.92	39.14
	Ulna	71.06	11.60	40.06
XVI. Oatmeal Skimmed Milk powder 10 c.c. coconut oil	Femur	73.79	11.91	45.45
	Femur-shaft	63.72	21.89	58.96
	Tibia	72.46	11.42	41.45
	Humerus	72.06	13.20	47.24
	Radius	69.69	14.22	46.89
	Ulna	69.16	14.22	45.80
XVII. Oatmeal 10 c.c. coconut	Femur	81.64	5.31	28.96
	Tibia	79.71	5.48	26.99
	Humerus	78.54	5.99	27.89
	Radius	75.73	7.40	30.48
	Ulna	74.61	7.87	31.02
XVIII. Ordinary diet + cod liver oil	Femur	59.99	22.20	55.51
	Femur-shaft	53.93	27.25	59.85
	Tibia	56.59	24.21	55.75
	Humerus	58.56	22.29	53.82
	Radius	55.04	24.21	56.70
	Ulna	54.64	23.31	51.39

4th Series of Experiments.

% Ca in			% P in			% Mg. in		
Fresh wgt.	Dry wgt.	Ash	Fresh wgt.	Dry wgt.	Ash	Fresh wgt.	Dry wgt.	Ash
3.55	14.36	34.11	1.32	5.33	12.66	0.08	0.32	0.76
5.68	18.80	35.98	1.85	6.13	11.72	0.13	0.40	0.83
3.71	13.71	36.18	1.86	6.90	18.20	0.09	0.32	0.84
3.86	14.65	36.31	1.96	7.44	18.44	0.08	0.29	0.72
3.86	13.82	35.33	1.95	6.99	17.86	0.07	0.26	0.66
4.08	14.08	35.16	2.02	6.97	17.39	0.07	0.25	0.61
4.27	16.31	35.88	1.84	5.15	11.27	0.06	0.24	0.53
8.09	21.79	36.94	2.23	6.01	10.19	0.12	0.32	0.55
4.60	16.70	40.31	1.98	7.18	17.31	0.06	0.23	0.56
4.97	17.78	37.65	2.27	8.11	17.17	0.08	0.27	0.57
5.34	17.63	37.59	2.43	8.03	17.12	0.08	0.26	0.55
5.43	17.50	38.19	2.43	8.00	17.47	0.08	0.25	0.54
1.70	9.24	31.93	0.79	4.32	14.93	0.03	0.18	0.62
1.95	9.62	35.58	0.70	3.46	12.88	0.03	0.15	0.56
2.15	9.99	35.82	1.11	5.17	18.54	0.04	0.16	0.59
2.56	10.51	34.54	1.18	4.87	15.97	0.04	0.17	0.56
2.78	10.96	35.37	1.24	4.87	15.70	0.05	0.19	0.63
8.00	20.02	36.07	4.02	10.04	18.09	0.15	0.37	0.67
10.16	22.06	36.84	5.40	11.73	19.60	0.17	0.38	0.63
9.17	21.12	37.87	4.04	9.30	16.67	0.15	0.35	0.62
8.16	19.70	36.60	4.02	9.70	18.01	0.15	0.37	0.69
9.01	21.10	37.21	4.02	9.41	16.59	0.16	0.36	0.64
8.86	19.52	37.98	4.12	9.08	17.66	0.15	0.32	0.62



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Fig. 1. Dog No. III. Control animal.



Fig. 2. Dog No. III. X-rays of the distal epiphyses of ulna and radius. Normal.



Fig. 3. Dog No. III. The rib junction of the control.

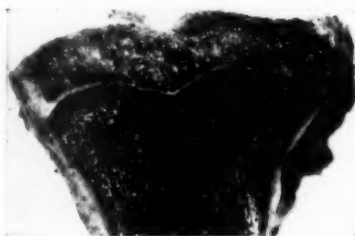


Fig. 4. Dog No. III. The upper epiphysis of tibia. Note the narrow epiphyseal line.



Fig. 5. Dog No. IV. Rickety dog at the commencement of treatment with cod-liver oil.



Fig. 6. Dog. No. IV. At the conclusion of the test. Treated with cod liver oil.



Fig. 7. Dog No. IV. X-rays at commencement of treatment with cod-liver oil.



Fig. 8. Dog No. IV. X-rays at the conclusion of cod-liver oil treatment. Note difference in epiphyseal lines in figs. 7 and 8.

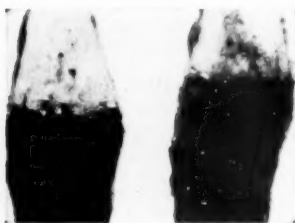


Fig. 9. No. IV. The rib junction in rickets treated with cod-liver oil.

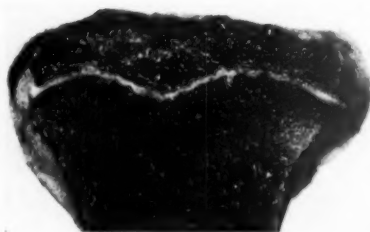


Fig. 10. Dog IV. Upper tibia epiphysis.



Fig. 11. Dog No. V. Rickets. Swelling of the distal epiphysis of ulna and radius. Plantigrade.

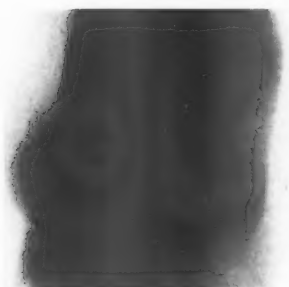


Fig. 12. Dog. No. V. X-rays of the distal epiphyses of ulna and radius. Severe rickets.

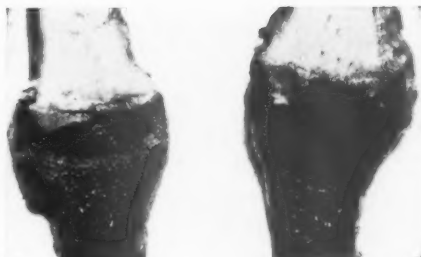


Fig. 13. The rib junction of the rachitic Dog No. V.

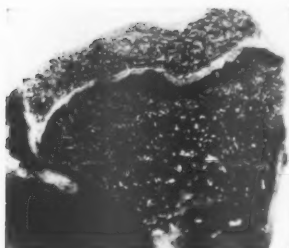


Fig. 14. The upper epiphysis of tibia of Dog No. V.



Fig. 15. Dog No. VI. Control for the 2nd series.

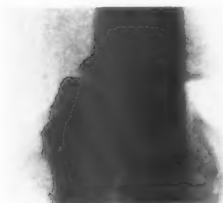


Fig. 16. Dog. No. VI. X-rays of the control Dog.



Fig. 17. Dog No. VI. The rib junction.



Fig. 18. Dog No. VI. Upper tibia epiphysis.



Fig. 19. The rachitic Dog No. VII, showing rickets with symptoms not so marked as in No. VIII.



Fig. 20. Dog No. VII. X-rays. Note the broad epiphyseal line.

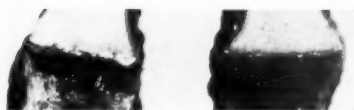


Fig. 21. Dog No. VII. The rib junction irregular.

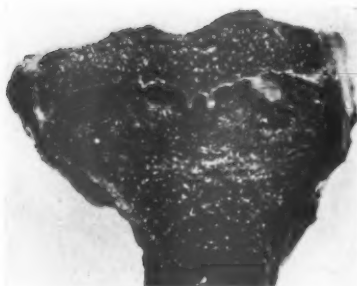


Fig. 22. Dog No. VII. Upper tibia epiphysis. Irregular, serrated, epiphyseal line.



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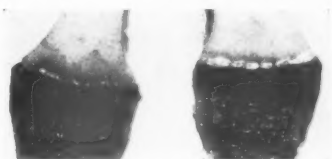


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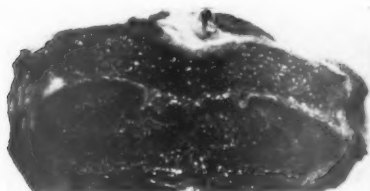


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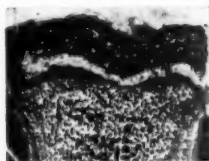


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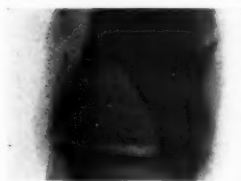


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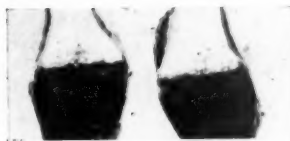


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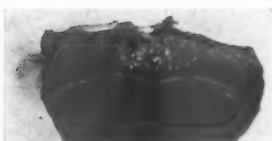


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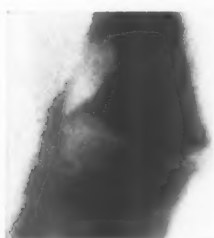


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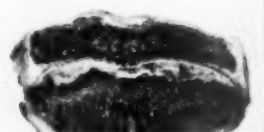


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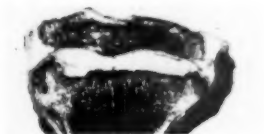


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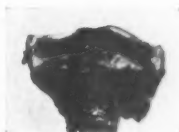


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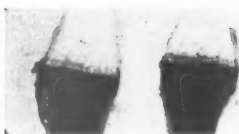


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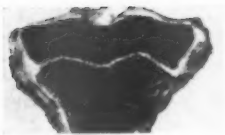


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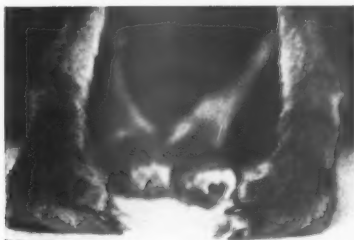


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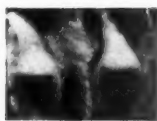


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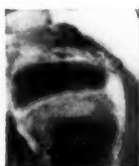


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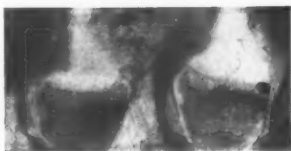


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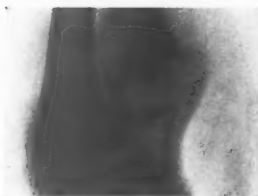


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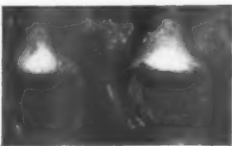


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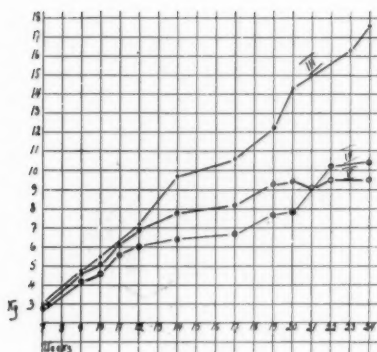


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Note the large weight of Control Animal No. III.

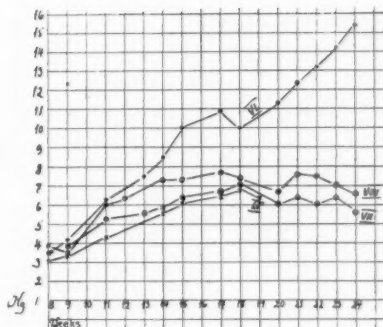


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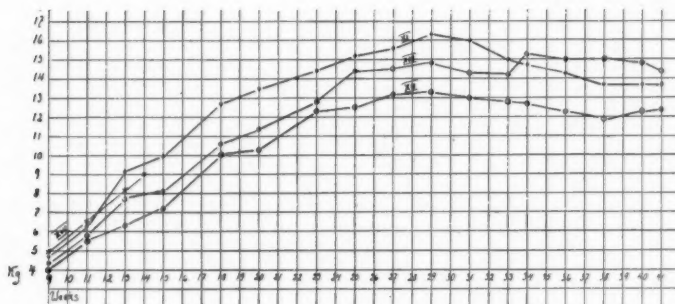


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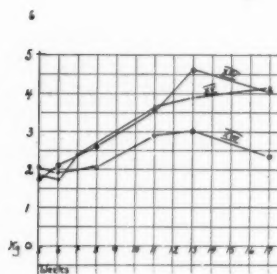


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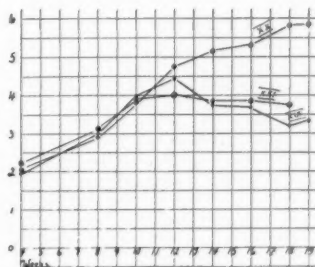


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STUDIES ON THE MINERAL
METABOLISM DURING PREGNANCY
AND LACTATION AND ITS BEARING ON
THE DISPOSITION TO RICKETS
AND DENTAL CARIES

BY

KIRSTEN UTHEIM TOVERUD

DR. MED. PEDIATRICIAN

AND

GUTTORM TOVERUD

DR. PHIL. DOCENT IN PEDODONTIA

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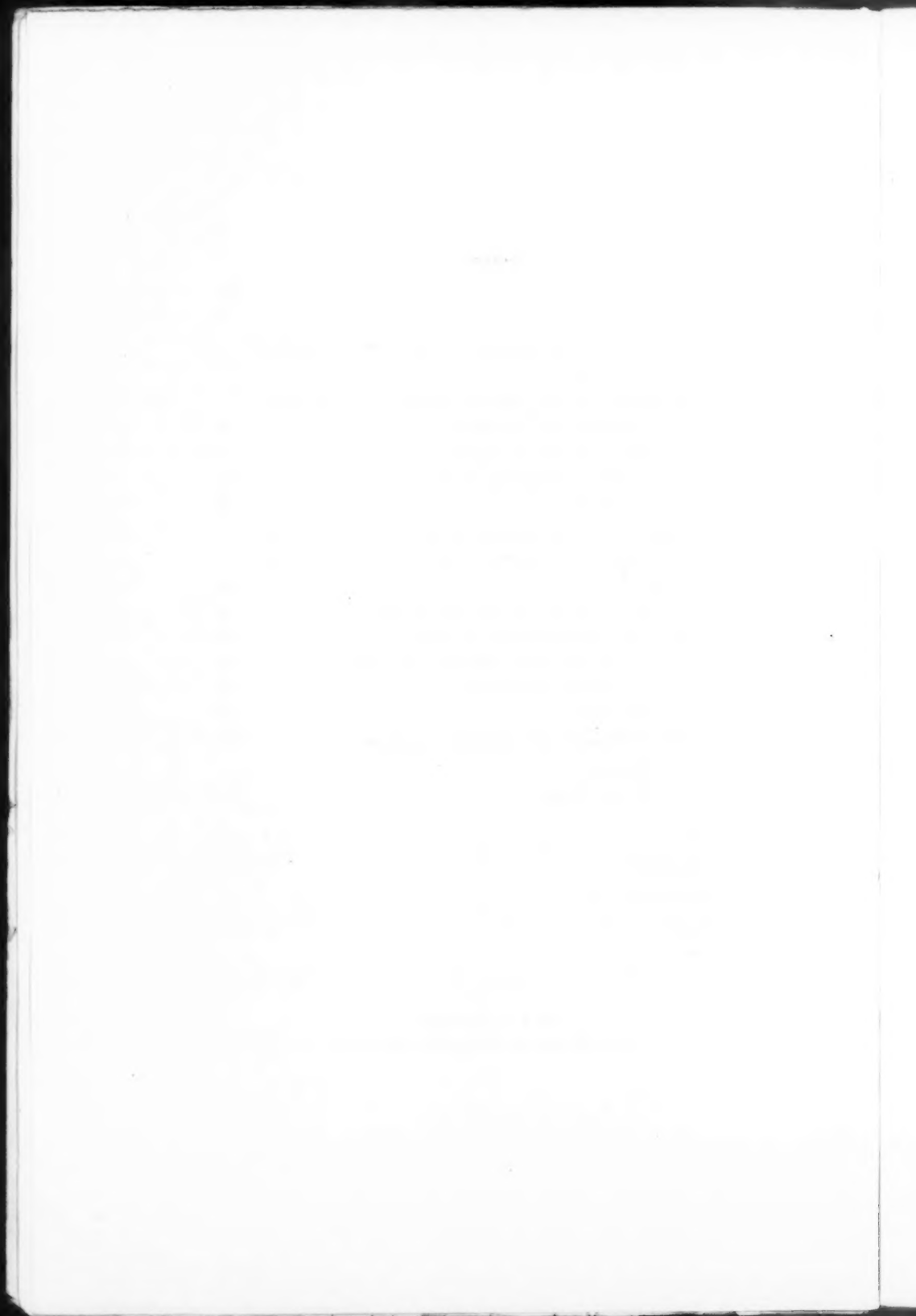
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I. Introduction.

To a certain extent we know most of the direct etiological factors in the development of rickets and dental caries. Nevertheless there are still many points in the question of the different disposition to these diseases which still are open to discussion. At least they have been difficult to explain on a strict scientific basis.

As regard to *rickets*, we find that the disposition to this disease vary considerably for different infants even belonging to the same family, born by the same mother, and the post-natal factors being practically alike. It is a fact that rickets particularly is associated with that period of the individual's life when growth is most rapid, namely the first two years, and the clinical symptoms of this disease are most pronounced in cases where the increase in weight has progressed most rapidly. Rickets we know, is not a specific disease just in artificially fed infants, but is well known also among breastfed infants. Furthermore we see from different statistics, that rickets, even nowadays, when we are quite well informed on child hygiene, still is a very frequent disease. According to ELIOT (1) for instance, it is found in 90 % of infants coming to New Haven dispensary in 1925, and clinical rickets *was found in all* the 197 breastfed infants examined by DE BUYS 1924 (2) in the first year of life. Any statistics from Norway for the last years we have not found. Furthermore the usual prophylactic work against rickets does not always seem to be effectiv. Even in fullterm infants a strictly controlled prophylaxis does not always prevent development of rickets as shown by ELIOT (1).

We know that premature infants and twins particularly are disposed to rickets even in such a degree that prevention in these cases in spite of a well regulated post natal diet is often unsuccessfull.

As regards to dental caries it is particularly the macro- and microscopical hypoplasia of the deciduous teeth and the 6 year molar which have to be mentioned in this connection.

These facts taken from the practical life point in the direction of a congenital disposition beeing present in some cases playing a considerable part in the development of these diseases. The old question of a hereditary, or, as we now rather call it, a congenital rickets, has once more to be discussed.

II. Brief Review of the Question: Disposition to Rickets and Dental Caries.

An hereditary factor in the development of rickets was once emphasized by SIEGERT (3).

A true heredity may perhaps not be considered. The question is whether or not a congenital factor is or may be a determining factor in development of this disease.

Some years ago one tried to solve this question by histological examination of bones from newborns: SCHMORL (4), WIELAND (5), with a completely negative result. However significant these examinations are, we have to remember, that they give no information as to the preceding feeding and hygiene of the mothers throughout pregnancy, a fact which may render these examinations somewhat less valuable for the question we are dealing with in this paper: the predisposition to rickets. Neither could a congenital rickets be found by taking Xrays of the epiphyses of newborn: A. F. HESS and WEINSTOCK (6), neither by chemical examinations of blood from newborn, HESS and MATZNER (7). The same remark has to be made as regards to these examinations, the authors give no information as to feeding and hygiene of the mothers throughout pregnancy.

YLLPÖ (8) however found by roentgenological investigation of the bones and epiphyseal centers of newly born premature infants that rickets was present in 5 of the 88 infants examined. No histological studies were performed. HESS (9) in his monograph on rickets expresses his present point of view as follows: 'It has been my experience in the course of an examination of the epiphyses of a large number of newly born infants, that peculiar and unexplained epiphyseal margins are

evident occasionally — epiphyses which instead of being sharp are slightly frayed with a tendency of cupping such as might be determined incipient rickets in later months».

In this connection it has to be mentioned that we can hardly think of the possibility of finding full developed clinical rickets in infants at birth, as we know that a rachitic process has to last for some time before clinical symptoms appear.

Nevertheless, a disposition to development of such a process may be present at birth, which clearly will be demonstrated by our experimental material presented below. With the word *disposition* we may then understand an anomaly in the infant's organism which in many cases may not be determined by our usual clinical methods, but by quantitative analyses of different components of the organism, particularly the mineral salts of bones and teeth.

Not only the above mentioned experiences from the practical life seem to show that a predisposition is present. But the rather scanty publications of an early manifestation of rickets point in the same direction, f. instance the case described by SCHMORL (4) with histological changes of rickets in an infant aged six weeks, and moreover that of DUNHAM (10). Here distinct clinical rickets was found in a full term 34 days old infant.

Many facts therefore point in the direction of the prenatal period with possible dietetic errors and poor hygienic conditions of the mother throughout pregnancy being of deciding influence on the disposition to rickets.

This problem has been discussed before and both experimental and clinical examinations have been performed in order to clear this point. HESS and WEINSTOCK (11) 1924 investigated whether or not rickets in young rats may be prevented by giving the mothers cod liver oil throughout the whole gestation period in addition to the usual ration. The youngs however developed rickets even if they were given a ricketogenic ratio after the nursing period.

The same apparently negative result these authors arrived at by clinical experiments: namely that rickets can not

be prevented in the infant by giving the mothers cod liver oil throughout the last 2 months of pregnancy even if the child is given entirely breastmilk after birth. The severity of the ricketic process however is influenced by such a procedure. The problem of rickets, these authors therefore believe, has to be solved by regulating the infants's feeding, that is in the postnatal period.

Another point of view is given by BYFIELDS and DANIELS (12), KORENCHESKY and CAR (13) and E. MELLANBY (14). By experiments on rats and dogs they have found that the prenatal period is of great influence as far as development of rickets in the youngs is concerned. They have particularly been interested in the anti-rachitic vitamin. This vitamin has been excluded from the mothers' diet during gestation and in such cases they have found earlier development of rickets in the youngs than in cases where the mother was given sufficient of this vitamin.

Mellanby has even shown that if two puppies, born by two such differently fed mothers during gestation and lactation are given a complete diet for 4 months and then a rickets producing diet, the disposing factor to rickets is still plainly present in the dog born by the mother with insufficient diet throughout gestation and lactation. When the dogs were 10 $\frac{1}{2}$ months old a big difference was noticed in these animals. A well developed rickets was found in the dog the mother of which had lived on a deficient diet while the control dog was quite normal.

As far as the other condition, *dental caries*, is concerned this as well may be said to be associated with the typical periods of growth in the individual's life: Childhood, puberty, pregnancy and lactation, all periods when considerable addition to the hard tissue takes place in the body, or when there is a great demand of mineral salts.

As for rickets there appear to be a distinct difference in the disposition to caries in the different individuals, even in

children belonging to the same family, born by the same mother and grown up under apparently the same hygienic conditions.

These facts point in the direction that factors may be present during the formation or calcification period of the teeth which may have a deciding influence on the resistance of the teeth to the carious process.

As early as 1895 WALKHOFF (15) writes: »Der Weg zur Einschränkung der Zahnkaries kann nur mit Erfolg beschriftet werden, wenn die *Prädisposition* der Zähne zivilisierter Nationen zur Karies nach Möglichkeit fortgeschafft wird. Die Prädisposition hat aber ihren *hauptsächlichen* Grund in den *Entwicklungsfehlern* der harten Zahngewebe».

M. MELLANBY (16) has also shown that there is a distinct relationship between the structure of the tooth and its resistance to caries. The more macro- and microscopical hypoplasia present in a tooth the less resistance to caries. The tables below demonstrate these conditions plainly.

Table 1. May Mellanby's Table on the Structure of Deciduous Teeth.

	Number examined	Normal		Slight hypoplasia		Hypoplasia and severe hypopl.	
		Number	Pet.	Number	Pet.	Number	Pet.
Incisors . .	236	115	49	87	37	34	14
Canines . .	156	12	8	59	38	85	54
I molars . .	249	17	7	49	20	183	73
II molars . .	395	5	1	27	7	263	92
Total . . .	1036	149	—	222	—	665	—
Average . .	—	—	14,4	—	21,4	—	64,2

In this connection it has to be remembered that the calcification of the crowns of the deciduous teeth take place during fetal period, from the 17th week to the end of this period. The calcification of the permanent teeth takes place

Table 2. May Mellanby's Table on the Relationship between Structure and Caries.
(Deciduous Teeth).

	Number examined	Good structure		Deficient structure	
		No caries	Caries	No caries	Caries
Incisors . . .	100	58	11	1	30
Canines . . .	70	5	0	25	40
Molars	466	2	11	2	451
Total	636	65	22	28	521

partly in the last months of fetal life (the 6 year molar), partly during the lactation and partly during childhood, what will appear from the diagrams below, see figs. 1 and 2.

From what is said above it is conceivable that the pregnancy period with the various factors which may disturb the metabolism during this time is of great direct importance for the development of the deciduous teeth and partly also for the 6 year molar, and thus for the resistance of these teeth to caries.

The great question is what dominating factors may be present during this time and in what way they may play a part. M. MELLANBY has especially emphasized the importance of the presence of sufficient antiricketic vitamin for the normal calcification process of the teeth in fetal life as well as in childhood. HOWE (17) and WALKHOFF (18) inter alia lay particular stress on the antiscorbutic vitamin, and RØSE (19) for instance, on the mineral substances.

Thus it seems to be evident that the diet during pregnancy is of great importance for the two diseases: *rickets* and *dental caries*. The authors mentioned above, however (with the exception of Korenchevsky, E. Mellanby) have chiefly concentrated their attention on one factor in this connection. Both diseases however dealt with in this paper mostly attack the hard tissues of the body: *bones* and *teeth*. Even if the vitamins

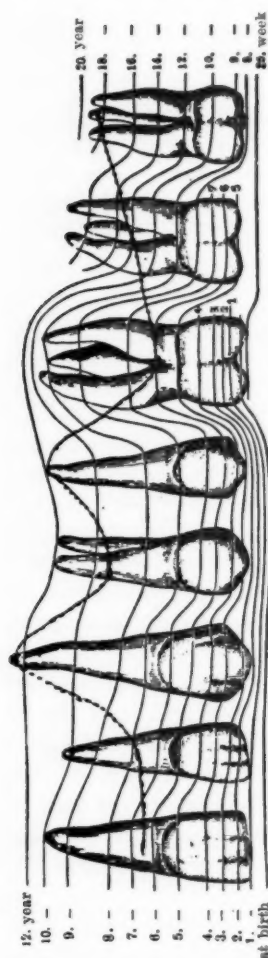


Fig. 1. The time of calcification of permanent teeth according to PIERCE.¹ The pointed line indicates the time of eruption of the teeth in relation to the calcification of the root. (Amoëdo).

play an important part in the ossification-process of the organism, this is just one side of the fact. The different mineral salts of which the teeth and bones consist have to be paid attention to as well. The factors playing part in a normal calcification process are several, and we do not perhaps know all of them yet. There are however some well established facts: an ample supply of minerals and calcifying vitamins, a surplus of base-giving foods and a normal functioning of the internal glands.

As far as the retention of Ca and P is concerned we know from the work of BROWN and SHOHL (20) that it is primarily dependent upon the salt constituents of the diet: »The calcium and phosphorus must be present in the diet in sufficient amounts and in correct relationship to each other before the rat can retain them in proper amounts and in correct relationship for normal bone deposition, vitamin or no vitamin.»

A certain minimum is always required of the different mineral salts to cover the daily need, and this minimum is highly increased throughout pregnancy where a great additio-

¹ According to own observations the calcification of the central incisor starts at 6th to 8th month after birth.

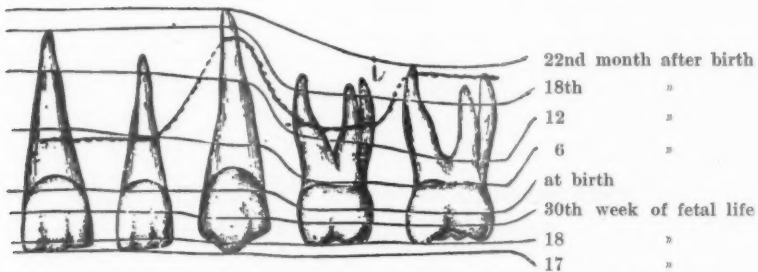


Fig. 2. The time of calcification of deciduous teeth according to PIERCE. The pointed line indicates the time of eruption in relation to the calcification of the root. (Amoëdo).

nal growth takes place, namely the development of the fetus. Therefore we have to ask if this minimum always is covered throughout pregnancy and also throughout lactation. We are thus led to consider the mineral metabolism of the pregnant and lactating mother to find out whether or not anomalies are present during these periods which may partly explain the great disposition to the two diseases discussed. A thorough study of the mineral metabolism seems therefore to be needed as the literature on this problem is rather scanty.

III. Investigations on the Mineral Metabolism of Women during Pregnancy and Lactation.

A. Short Survey of Previous Literature.

In the literature we will often find remarks about possible disturbances in the calcium and phosphorus metabolism during pregnancy and lactation. These more vague suppositions seemed earlier to be based chiefly on the theoretical calculations alone as the very few exact metabolism studies at disposal until the very last years show that quite normal balances of Ca and P exist during these two periods.

SILLEVIS (21) 1903 is evidently the first who has performed mineral metabolism studies on a clinical material during pregnancy. He found a positive P balance as well as a positive N balance in three primiparae women. The french gynecologist BAR (22) performing similar investigations also found a good positive balance for P and N. The nitrogen metabolism during pregnancy has been thoroughly studied by several investigators and nearly all of them have found a good positive balance throughout pregnancy.

In 1910 HOFFSTRÖM (23) published a very thorough investigation on the metabolism of Ca, P and Mg in one woman from the 17th week of pregnancy until delivery. The result of this investigation showed that the woman passed the pregnancy with a good positive balance for all three elements. Just a few negative balance-periods were found in the first part of pregnancy. The daily Ca intake by this woman ranged from 1,2—2,4 gm. and the daily P intake from 1,7—2,4 gm. LANDSBERG (24) as well, has found a positive Ca and P balance in 14 women examined from the 2nd to the 10th month of preg-

nancy. The daily Ca intake ranged in these experiments from 1,8—2,9 gm. and the daily P intake from 2,1—3,1 gm.

About one year after the first preliminary report of our own experiments was published (25) there appeared some papers by Mc. COONS and BLUNT (26), MACY, HUNSCHER, NIMS, Mc. COSH (27), HUNSCHER (28) and MACY, HUNSCHER, Mc. COSH and NIMS (29) on this subject. In the studies by Coons and Blunt the Ca intake ranged from 0,6—1,7 gm. and in 8 of 9 women the daily Ca intake was below 1 gm. The authors found that the daily retention of Ca did not cover the need of the fetus. In one of the other experiments (27) a negative Ca balance as recorded in 5 metabolism experiments on a daily Ca intake ranging from 1,5—2,7 gm., and a negative P balance was recorded twice on a daily P intake ranging from 1,5—3 gm. It has to be mentioned that these three women were multiparae and had just previous to the experiments gone through a long and heavy lactation period. In the studies by HUNSCHER (28) a negative Ca and P balance was found in the middle of the lactation period, on a very high daily Ca intake of 2,8—4,4 gm. Ca and on a daily P intake of 2,9—4,3 gm. These women, also, had been under great biological demand just previous to the experiments. In another of these papers (29) is demonstrated the effect of cod liver oil and yeast on this negative balance. The balance turned to a positive one in some cases and in other cases it was somewhat improved. These papers will be discussed later.

While the mineral metabolism studies performed during pregnancy are rather few, the studies on the mineral salt content of the blood have been more numerous. The earlier investigations show a higher Ca content of the blood in pregnant than in non pregnant women. LAMERS (30) f. inst. reported a Ca content of 8 mgm. pr. 100 cc. serum in non pregnant, and 11,6 mgm. in pregnant women. In lactating women too an increased amount of Ca in the blood has been found by the same author. UNDERHILL and DIMICK (31) have arrived at the same result. Most of the investigators from the recent years, however, have found a lowered Ca content

of blood serum during the last part of pregnancy. MAZZOCCO and MORON (32) have thus found 9,19 mgm. Ca in non pregnant and 8,77 mgm. Ca pr. 100 cc. serum in pregnant women. WIDDOWS (33) reports the following figures: 11,1 mgm. Ca in the 3rd and 4th month of pregnancy, and 9,4 mgm. in the 8th and 9th month. Similar figures are also reported by de WESSELOW (34), BOGERT and PLASS (35) and KREBS and BRIGGS (36).

The calcium content of the saliva has also been investigated during pregnancy. RICKERT and PALMERLEE (37) have demonstrated a lowering from 7,6 mgm. Ca pr. 100 cc. saliva in non pregnant to 4,3 mgm. in pregnant women one month before delivery. BECKS' investigations (38) show a value of 12,14 mgm. pct. Ca in physiological normal saliva and of 6,18 during the last months of pregnancy.

While the few metabolism studies performed in earlier years do not point in the direction of any anomaly in the calcium metabolism during pregnancy, the metabolism studies from the last years and most of the blood analyses and the saliva analyses point in the direction that such is the case. The histological and the chemical examinations of bones from pregnant women point in the same direction. HANAU (39) has demonstrated enlarged osteoid zones in different bones throughout the body, particularly in the pelvic bones. Mc. CRUDDEN (40) and WHITE (41) have found a lowering of Ca of the bones from women suffering of osteomalacia during pregnancy.

In a recent publication of VIGNES (42) is emphasized that disturbance in the Ca-metabolism are rather frequent during pregnancy and he attributes many of the common pathological symptoms of this period as dental caries, osteomalacia, tetany, vomiting and eclampsia to such a disturbance in the calcium metabolism.

Many investigators as well as clinicians do realise that in many cases a similar sort of disturbance in the calcium metabolism during pregnancy may exist. The cause of this disturbances, however, is not clear. The possibility of a too

low calcium intake has especially been discussed f. inst. by LOEW (43). The earlier metabolism experiments performed in this connection, however, have given a positive balance showing a sufficient intake. On the other hand the more recent examinations by Mc. Coons and Blunt where the Ca intake of 8 out of 9 women was below 1 gm. daily gave often a negative balance. An important question is whether or not a Ca and P intake used in the work of Hoffström and Landsberg may be considered as an average intake. It has to be mentioned that the daily Ca intake of 1,7 to 2,0 gm. is an intake so high that very few pregnant mothers at least in this country take such an amount. About 70—80 % of the daily Ca intake is arrived from the milk. Considering the low milk consume common now a days at least in Norway, such high figures as 1,7 gm. Ca is very seldom reached. According to the statistics of the department of Public health of Oslo the milk intake has not even reached 500 gm. pr. individual and day. Neither in cities nor in rural districts we may consider such a high intake as one liter which contains about 1,2 gm. Ca as common. The other foodstuffs besides milk and milkproducts are low in Ca. Fruit and vegetables, which next to milk are the best sources of Ca, do not take a broad place in the common household in this country, mostly on account of economical difficulties. By examinations of above 100 mothers from the east-end and west-end of Oslo, we found that the average intake of Ca very seldom exceeded 1 gm. daily. The most common figure was about 0,6—0,7 gm. daily. As we have seen, the intake of most of the mothers from Coons and Blunt's material was below 1 gm. even in a country (U. S. A.) where fruit and vegetables are easily accessible. The very high intake of the mothers described by Hunscher and coworkers was evidently arrived at by regulating the diet.

The question then arises whether or not a daily intake of 0,6 to 1,0 gm. Ca is sufficient to cover the need in this period. During pregnancy two individuals are to be provided for, the mother and the fetus. The Ca need of an adult person un-

der usual conditions has to be considered just as well as the need of the fetus during different periods of development.

The figures given by SHERMAN (44) of 0,67 gm. Ca and 1,44 gm. P pr. day for a person af 70 kg. seem to be universally recognized. For a woman with an average body weight, the figures will be 0,54 gm. Ca and 1,15 gm. P. As regards the need of the fetus we have perhaps the most complete analyses from MICHEL (45) on the mineral content of the fetus at different ages, see table no. 3.

Table 3. The Mineral Content of the Fetus at Different Ages according to Michel.

Age of fetus	Ca gm.	P gm.	Mg gm.
4 months	1,898	1,248	0,069
5 "	2,530	1,641	0,085
6 "	4,080	2,440	0,133
7 "	5,885	3,525	0,190
At birth	33,240	18,685	0,812

The average retention pr. day calculated according to Michel we will see from table no. 4.

Table 4. The Average Daily Retention of the Fetus according to Michel.

Age of fetus	Ca gm.	P gm.	Mg gm.
Up to 4th month	0,015	0,010	0,001
From 4th to 5th month . .	0,021	0,013	0,001
" 5th " 6th " . .	0,050	0,026	0,002
" 6th " 7th " . .	0,060	0,036	0,002
" 7th month to birth . .	0,456	0,254	0,010

GIVENS and MACY (46) give somewhat lower figures, other authors even higher than Michel. From the figures of Sher-

man and Michel it is conceivable that a Ca intake of 0.6—0.7 gm. just cover the need of the mother and might perhaps be sufficient for the fetus during the first months of pregnancy. But with an average retention by the fetus of 0.456 gm. daily, such an intake is far from sufficient.

Thus we find that a Ca and P intake of the pregnant woman in the work by Hoffström and Landsberg far exceeded the amount common in the food of most pregnant women, at least in this country. According to the figures of Sherman and Michel we find it quite natural that the balance of these women was positive with an intake sometimes reaching the double of the theoretical calculated amount, providing the food otherwise was sufficient. This fact: a positive Ca and P balance in all the women examined on such a high intake ought to be emphasized as we thus may see that the mineral metabolism even during pregnancy may be kept on a normal level when the mineral intake is sufficiently high.

In the women examined by Hunscher and coworkers the Ca balance was negative in spite of a very high Ca intake. In this material other factors may play a dominant rôle, *f. inst.* the great biological demand previous to the experiment. See discussion below. We know there are many factors playing a part in the calcium metabolism. Of these factors the vitamin content of the food, the acid-base balance of the diet, the Ca:P relation in the food, the internal glands are perhaps of the greatest importance. These factors which are of the same importance, and even more so during pregnancy, than during usual conditions, will be discussed later in the paper.

Summing up what is pointed out in this brief survey, we may say that symptoms during pregnancy and lactation are described which point in the direction of a disturbance being present during this time. On the other hand we have reported direct metabolism experiments (Hoffström and Landsberg) which do not reveal any disturbance (a. Ca intake, however, above the usual one).

Our own first experiments from 1927 and those of Coons

and Blunt from 1930 on an intake below 1 gm. and furthermore those by Hunscher and coworkers on an intake even higher, point in the direction of a disturbance existing quite often in the mineral metabolism during pregnancy.

In order to throw more light on this question we have continued our investigations, and as the first part of our experiments was published just in Norwegian we are here presenting our complete material.

B. Own Investigations on Women.

The investigations to be described were started in the fall 1927 and have gone on for 3 $\frac{1}{2}$ years at the Physiological Department of the University and partly at the Dental School of Norway. The women examined have lived in a home for expecting mothers in Oslo where the head nurse was especially trained in metabolism work.

The studies have been arranged as follows:

The metabolism period has mostly lasted 4 days, and the women have during this time been given the food commonly used in the home. No study has been performed until the women had stayed at least 1 week in the home. As may be seen from the tables, the usual diet was sometimes changed. A metabolism study on the new diet, however, was never performed until 1 week after the change had taken place.

The amount eaten of the different food materials was carefully weighed and measured and the Ca, P and Mg of the food were mostly determined directly by analyses. Just a few articles with rather constant values have been calculated according to RAGNAR BERGS tables of food analyses (47). The urine was collected from 8 o'clock in the morning the 1st day till 8 o'clock in the morning the 5th day and the stools were separated by coal at the beginning and at the end of the experiment.

The usual diet in the home has been:

Breakfast: Bread of mostly whole grain with butter and marmelade or cheese. Coffee.

Forenoon: Oatmeal with milk.

Dinner: Meat or fish with potatoes and vegetables. Soup, fruitsoup or soup of milk or cream of rice.

Afternoon: Coffee with cakes.

Supper: Oatmeal with milk, or salt herring with potatoes, or bread and butter, cheese, jam and tea.

The average daily intake of milk did not exceed 500—600 cc. pr. woman.

During the experiments the women have done usual housework besides garden work spring, summer, and fall.

The food articles, urine and feces have been ashed on dry way, and the Ca, P and Mg have been determined in the hydrochloric acid solution according to the same methods as used in earlier work, TOVERUD (48).

From the 44 metabolism experiments performed during pregnancy on 17 women living on the usual diet of the home, or with a prescribed addition it is to be seen that a negative Ca and P balance are found in the majority of cases, see table 5, p. 22. As far as the Ca is concerned we find that no woman showed a positive balance in the two last months of pregnancy unless the Ca intake had reached the value of 1,6 gm. pr. day.

According to these investigations we should be able to put up as an »optimum intake», that is the intake under otherwise normal conditions which on the basis of this material supposedly would give a positive balance of Ca and P during the two last months of pregnancy: at least 1,6 gm. of Ca and P pr. day.

That this holds true may be seen from the result of the metabolism experiments after regulating the diet of the home, see table 7, p. 35, and table 8, p. 36. These figures are closely up to those found in the work of Hoffström and Landsberg. It is, however, evident from our metabolism experiments as well as from our examination of a number of mothers in Oslo that such high figures are just rarely found in the diet of an average Norwegian woman. The high amount of Ca and P is hardly met with unless the diet is regulated particularly in this respect.

Table 5. Metabolism Studies on Women during Pregnancy.

Woman no.	Month of pregn.	Diet	Minerals studied gm.	Intake	O u t p u t			Balance	
					Urine	Feces	Total	Without count. fet.	Count. fet.
1	8	Ordinary	Ca:	1,1712	0,2137	0,5056	0,7193	+ 0,4519	÷ 0,0041
			P:	1,1003	0,5786	0,4000	1,0386	+ 0,0617	÷ 0,1923
			Mg:	0,3394	0,0564	0,1303	0,1367	+ 0,1527	+ 0,1427
1	9	Ordinary	Ca:	0,7555	0,2585	0,4556	0,6941	+ 0,0614	÷ 0,3946
			P:	1,0560	0,8433	0,5640	1,4073	÷ 0,3513	÷ 0,6053
			Mg:	0,3639	0,1088	0,2755	0,3793	÷ 0,0154	÷ 0,0254
2	7	Ordinary	Ca:	0,7152	0,1787	0,5000	0,6787	+ 0,0865	÷ 0,4195
			P:	0,9825	0,7466	0,5467	1,2933	÷ 0,3108	÷ 0,5643
			Mg:	0,2933	0,0833	0,2217	0,3050	÷ 0,0117	÷ 0,0217
2	7 1/2	Ordinary	Ca:	0,5819	0,2116	0,4967	0,7083	÷ 0,1264	÷ 0,3824
			P:	0,6972	0,8437	0,4643	1,3080	÷ 0,6108	÷ 0,8643
			Mg:	0,2171	0,0893	0,1750	0,2643	÷ 0,0472	÷ 0,0572
2	8	Ordinary + 1 l. milk daily	Ca:	1,6961	0,1730	1,0700	1,2430	+ 0,4531	÷ 0,0029
			P:	1,4480	0,8666	0,5717	1,4383	+ 0,0097	÷ 0,2443
			Mg:	0,3044	0,0837	0,2008	0,2845	+ 0,0199	+ 0,0099
2	9	Ordinary + 1 l. milk + 20 cc. cod liver oil daily	Ca:	1,7311	0,2093	0,8450	1,0543	+ 0,6768	+ 0,2208
			P:	1,8833	0,8017	0,5833	1,4750	+ 0,4113	+ 0,1573
			Mg:	0,3630	0,0917	0,2156	0,3073	+ 0,0617	+ 0,0517

3	8	Ordinary	Ca:	1,3372	0,1253	1,0367	1,1620	+0,1732	÷-0,2868
			P:	1,5112	0,7375	0,5733	1,3108	+0,2004	÷-0,0536
			Mg:	0,3342	0,1073	0,2125	0,3198	+0,0144	+0,0044
3	8 1/2	Ordinary + 0.546 gm. Ca (Kalan) daily	Ca:	1,6684	0,1113	1,0667	1,1480	+0,5204	+0,0644
			P:	1,5218	0,8733	0,7684	1,6867	÷-0,1149	÷-0,3689
			Mg:	0,3845	0,1133	0,3529	0,3682	+0,0133	+0,0033
3	9	As above + 20 cc. cod liver oil daily	Ca:	1,6684	0,0917	1,1600	1,2517	+0,4167	÷-0,0393
			P:	1,5218	0,7533	0,8259	1,5792	÷-0,0574	÷-0,3114
			Mg:	0,3845	0,1100	0,1360	0,2460	+0,1355	+0,1255
4	7	Ordinary	Ca:	1,0905	0,1206	0,7617	0,8823	+0,1982	÷-0,2578
			P:	1,4187	0,4983	0,5667	1,0650	+0,3337	+0,0907
			Mg:	0,3455	0,0720	0,2102	0,2912	+0,0543	+0,0443
4	7 1/2	Ordinary	Ca:	0,9940	0,1127	0,6175	0,7302	+0,2638	÷-0,1922
			P:	1,3903	0,5400	0,4667	1,0257	+0,3636	+0,1066
			Mg:	0,5027	0,0640	0,1840	0,2480	+0,2547	+0,2447
4	8	Ordinary	Ca:	0,6907	0,0505	0,5300	0,5805	+0,1102	÷-0,3458
			P:	0,8802	0,4100	0,2733	0,6803	+0,1439	÷-0,1101
			Mg:	0,2186	0,0597	0,1058	0,1655	+0,0531	+0,0431
4	8 1/2	The same as by 7 1/2 month	Ca:	0,9940	0,0408	0,8667	1,0275	÷-0,0335	÷-0,4805
			P:	1,3903	0,5467	0,5100	1,0567	+0,3336	+0,0796
			Mg:	0,5027			0,3467	+0,1560	+0,1460
5	3	Ordinary	Ca:	1,0261	0,2765	0,5175	0,7940	+0,2321	
			P:	1,3648	0,4867	0,2103	0,6970	+0,6678	
			Mg:	0,3548	0,0513	0,0904	0,1417	+0,2131	

Woman no.	Month of pregn.	Diet	Minerals studied gm.	Intake	O u t p u t			Balance	
					Urine	Feces	Total	Without count. fet.	Count. fet.
5	4	Ordinary	Ca:	1,1298	0,2907	0,5893	0,8790	+ 0,2503	+ 0,2553
			P:	1,9991	0,5383	0,2484	0,7817	+ 0,6174	+ 0,6074
			Mg:	0,3514	0,0577	0,1933	0,2530	+ 0,0986	+ 0,0976
*5	5	Ordinary	Ca:	0,9385	0,3400	0,5461	0,8861	+ 0,0524	+ 0,0314
			P:	1,1900	0,4875	0,3863	0,8738	+ 0,3102	+ 0,3092
			Mg:	0,3062	0,0596	0,1145	0,1741	+ 0,1321	+ 0,1311
*5	6 1/2	Ordinary	Ca:	0,6601	0,4125	0,5875	1,0000	÷ 0,0009	÷ 0,0009
			P:	1,2632	0,6550	0,3825	1,0375	+ 0,2257	+ 0,1897
			Mg:	0,3336	0,0724	0,3050	0,3773	÷ 0,0487	÷ 0,0457
5	7 1/2	Ordinary	Ca:	0,6718	0,3698	0,3062	0,6760	÷ 0,0042	÷ 0,4602
			P:	1,0045	0,5075	0,3175	0,8250	+ 0,1795	÷ 0,0745
			Mg:	0,2704	0,0588	0,0692	0,1280	+ 0,1424	+ 0,1324
5	8	Ordinary + 20 cc. cod liver oil daily	Ca:	0,8460	0,4363	0,4362	0,8725	÷ 0,0265	÷ 0,4825
			P:	1,0797	0,6444	0,3996	1,0440	+ 0,0837	÷ 0,2183
			Mg:	0,3049	0,0575	0,0486	0,1011	+ 0,2088	+ 0,1988
5	8 1/2	Ordinary + 1 l. milk daily	Ca:	1,4808	0,4488	0,7852	1,2290	+ 0,2518	÷ 0,2042
			P:	1,4039	0,8500	0,5212	1,3712	+ 0,0327	÷ 0,2213
			Mg:	0,3541	0,0689	0,0798	0,1782	+ 0,1759	+ 0,1659

*6	6	Ordinary	Ca: P: Mg:	1,0518 1,0652 0,3760	0,2552 0,4100 0,0555	0,8588 0,6950 0,0862	1,1140 1,1050 0,1417	÷ 0,0622 ÷ 0,0898 + 0,2333	÷ 0,1222 ÷ 0,0758 + 0,2313
7	8	Ordinary	Ca: P: Mg:	1,4505 1,4320 0,4198	0,2142 0,8682 0,0541	1,5000 0,8130 0,1425	1,7142 1,6792 0,1966	÷ 0,2687 ÷ 0,2472 + 0,2232	÷ 0,7197 ÷ 0,5012 + 0,2132
7	8 1/2	Ordinary + 20 cc. cod liver oil daily	Ca: P: Mg:	1,4311 1,5398 0,3316	0,1875 0,7700 0,0607	1,4725 0,6682 0,1140	1,3600 1,4382 0,1747	+ 0,0711 + 0,1016 + 0,1569	÷ 0,3849 ÷ 0,1524 + 0,1469
7	9	As above + 1 l. milk daily	Ca: P: Mg:	1,6502 1,9085 0,4282	0,2415 0,8900 0,0887	1,0010 0,5025 0,2125	1,2425 1,3925 0,3012	+ 0,4077 + 0,5160 + 0,1270	÷ 0,0483 + 0,2620 + 0,1170
8	8	Ordinary	Ca: P: Mg:	1,6918 1,9765 0,4164	0,3119 0,8063 0,0981	0,7000 0,4337 0,1578	1,0119 1,2400 0,2559	+ 0,6799 + 0,7365 + 0,1605	+ 0,2289 + 0,4825 + 0,1505
8	8 1/2	Ordinary	Ca: P: Mg:	1,4217 1,3737 0,2980	0,2292 0,8005 0,1080	0,7700 0,2750 0,0929	0,9992 1,0775 0,2009	+ 0,4225 + 0,2932 + 0,0971	÷ 0,0685 + 0,0422 + 0,0871
9	7 1/2	Ordinary	Ca: P: Mg:	0,8157 0,9662 0,2063	0,1105 0,6725 0,1137	0,6787 0,4423 0,0615	0,7892 1,1148 0,1652	+ 0,0265 ÷ 0,1486 + 0,0411	÷ 0,4295 ÷ 0,4026 + 0,0311
10	8	Ordinary	Ca: P: Mg:	0,9996 1,7559 0,6884	0,4350 0,3000 0,1180	0,5325 0,4275 0,1800	0,9675 1,2275 0,2980	+ 0,0311 + 0,5284 + 0,3904	÷ 0,4249 + 0,2744 + 0,3804

Woman no.	Month of pregn.	Diet	Minerals studied gm.	Intake	O u t p u t			Balance	
					Urine	Feces	Total	Without count. fet.	Count. fet.
10	8 1/3	Ordinary + 15 cc. "Calbifos" = 0,1215 gm. Ca + 0,2925 gm. P daily	Ca:	1,6782	0,5325	0,8725	1,4050	+ 0,2732	÷ - 0,1828
			P:	2,1132	0,9000	0,6728	1,5728	+ 0,5404	+ 0,2864
			Mg:	0,3932	0,1300	0,2400	0,3700	+ 0,0232	+ 0,0132
10	9	The same as in the first experiment + 45 cc. "Calbifos" = 0,3645 gm. Ca + 0,8775 gm. P daily	Ca:	1,3631	0,4675	0,6838	1,1513	+ 0,2118	÷ - 0,2442
			P:	2,6334	1,0750	0,5812	1,6562	+ 0,9772	+ 0,7232
			Mg:	0,6884	0,1175	0,2550	0,3725	+ 0,3159	+ 0,3059
* 11	6 1/3	Ordinary	Ca:	0,9135	0,1838	1,1125	1,2963	÷ - 0,3828	÷ - 0,4427
			P:	1,6067	0,7200	0,4580	1,1780	+ 0,4287	+ 0,3927
			Mg:	0,3137	0,0907	0,2065	0,2972	+ 0,0165	+ 0,0145
* 11	7	As above + 10 cc. cod liver oil daily	Ca:	0,9135	0,2635	0,6550	0,9185	÷ - 0,0080	÷ - 0,4590
			P:	1,6067	0,6188	0,4355	1,0488	+ 0,5579	+ 0,3039
			Mg:	0,3137	0,0792	0,1662	0,2454	+ 0,0683	+ 0,0583
11	8	As above	Ca:	0,9135	0,2275	0,7875	1,0150	÷ - 0,1015	÷ - 0,5575
			P:	1,6067	0,4300	0,4507	0,8807	+ 0,7260	+ 0,4720
			Mg:	0,3137	0,0630	0,2002	0,2632	+ 0,0505	+ 0,0405
12	8	Ordinary	Ca:	0,7522	0,0608	0,4625	0,5233	+ 0,2289	÷ - 0,2271
			P:	1,0288	0,3925	0,3150	0,7075	+ 0,3213	+ 0,0673
			Mg:	0,2503	0,0505	0,1150	0,1655	+ 0,0848	+ 0,0748

Ca:	1,1620	0,1525	0,8650	1,0175	+ 0,1445	+ 0,0845
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*13	6 1/2	Ordinary	Ca:	1,1620	0,1525	0,8650	1,0175	+ 0,1445	+ 0,0845
			P:	1,4505	0,5650	0,4850	1,0500	+ 0,4005	+ 0,3745
			Mg:	0,3300	0,0720	0,1738	0,2458	+ 0,0982	+ 0,0912
*13	7	The same as above + 10 cc. cod liver oil daily	Ca:	1,1620	0,1945	0,6075	0,8020	+ 0,3600	÷ 0,0660
			P:	1,4505	0,6748	0,3643	1,0391	+ 0,4114	+ 0,1574
			Mg:	0,3300	0,1008	0,1362	0,2370	+ 0,1020	+ 0,0920
13	8	Ordinary. (The same as in the I. experiment)	Ca:	1,2105	0,1782	1,4675	1,6157	÷ 0,4262	÷ 0,3822
			P:	1,4645	0,6002	0,6656	1,2658	+ 0,1987	÷ 0,0653
			Mg:	0,3440	0,0829	0,1850	0,2679	+ 0,0761	+ 0,0661
13	8 1/2	Ordinary + 10 drops "Vi- gantol" daily	Ca:	1,1282	0,1873	0,9097	1,0970	+ 0,0312	÷ 0,4248
			P:	1,3417	0,5556	0,4202	0,9758	+ 0,3659	+ 0,1119
			Mg:	0,3272	0,0604	0,1220	0,1824	+ 0,1448	+ 0,1348
15	8	Ordinary	Ca:	0,807	0,400	0,705	1,105	÷ 0,298	÷ 0,754
			P:	1,269	0,668	0,388	1,056	+ 0,213	÷ 0,041
			Mg:	0,289	0,087	0,181	0,268	+ 0,021	+ 0,011
15	8 1/2	Ordinary + 10 drops "Vigantol" daily	Ca:	0,807	0,380	0,690	1,070	÷ 0,263	÷ 0,719
			P:	1,269	0,692	0,355	1,047	+ 0,222	÷ 0,032
			Mg:	0,289	0,074	0,166	0,240	+ 0,049	+ 0,039
16	8	Ordinary	Ca:	1,155	0,445	0,467	0,912	+ 0,243	÷ 0,213
			P:	1,676	0,772	0,273	1,045	+ 0,631	+ 0,377
			Mg:	0,362	0,104	0,125	0,229	+ 0,133	+ 0,123
16	8 1/2	Ordinary + 10 drops "Vigantol" daily.	Ca:	1,155	0,380	0,460	0,840	+ 0,315	÷ 0,141
			P:	1,676	1,005	0,317	1,322	+ 0,353	+ 0,099
			Mg:	0,362	0,082	0,147	0,230	+ 0,132	+ 0,122

Woman no.	Month of pregn.	Diet	Minerals studied gm.	Intake	O u t p u t			Balance	
					Urine	Feces	Total	Without count. fet.	Count. fet.
17	6	Ordinary	Ca:	1,390	0,412	1,093	1,480	÷0,090	÷0,150
			P:	0,711	0,782	0,385	1,170	÷0,469	÷0,495
			Mg:	0,186	0,114	0,114	0,228	÷0,042	÷0,044
17	6 1/2	Ordinary + 10 drops "Vigantol" daily	Ca:	1,390	0,315	0,770	1,085	+0,305	+0,245
			P:	0,711	0,662	0,394	1,056	÷0,345	÷0,381
			Mg:	0,186	0,072	0,094	0,166	+0,020	+0,022

* According to the tables of Michel, p. 18, a marked increase in the Ca and P retention is noticed from the 6th to 7th month of fetal life. Being fully aware that the increase in retention takes place more gradually, the above mentioned figures, based on analyses, are nevertheless used in want of more detailed ones. In evaluating the results this has to be considered.

Of the 12 metabolism studies performed on 6 women during lactation, 4 experiments show a negative Ca balance and 6 a negative P balance, see table 6, p. 30.

As is evident from the tables we have tried to change a negative balance into a positive one by increasing the amount of minerals in the food mostly by increasing the milk intake, but also some times by adding a calcium salt to the diet, in these experiments »Kalzan.»

As mentioned above no metabolism studies have been performed unless the woman was kept at least 1 week on this altered diet.

The tables demonstrate plainly that the negative balance has passed over to a positive one in many cases by an increase in the mineral intake. In the cases where this is not true, the balance has become much less negative.

The food given to these women has not only been low in Ca and P but relatively low in fatsoluble vitamins. It might be supposed that the negative balance of these women was due to the low content of vitamin D in the food. Therefore, 20 cc. (in 1927), and later 10 cc. of a potent cod liver oil¹ have been given every day to some of the women showing a negative balance. The tables give information as to the result. Such an addition is evidently of value for woman no. 2 and no. 7. In the other cases addition of fatsoluble vitamins have not influenced the balance.

In case no. 2, p. 22 the balance in the fourth experiment is turned to a positive one both for Ca and P. We see, however, that the intake of both of the minerals too are increased besides the addition of cod liver oil.

In case no. 3 we find after addition of cod liver oil in the 3rd experiment with constant Ca intake the Ca balance changed from a slightly positive one to a slightly negative one. As far as P is concerned the negative balance was decreased somewhat.

¹ We are indebted to the professors dr. Poulsson and dr. Langfeldt for the standardized samples of cod liver oil used to the women and dogs.



Table 6. Metabolism Studies during Lactation.

Woman no.	Month of lact.	Diet	Minerals studied gm.	O u t p u t			Total	Balance
				Urine	Feces	Secreted milk		
1	2	Ordinary	Ca:	0,1528	0,3909	0,2283	0,7665	÷-0,0104
			P:	0,6327	0,4893	0,2117	1,3337	÷-0,0320
			Mg:	0,0676	0,3171	0,0347	0,3194	+0,0651
1	2 1/2	Ordinary + 1 liter milk daily	Ca:	0,2977	0,9100	0,2100	1,4177	+0,4171
			P:	0,9650	0,6140	0,2000	1,7790	+0,2119
			Mg:	0,0323	0,2585	0,0325	0,3743	+0,3665
1	3	Ordinary + 1 liter milk + 0,546 gm. Ca (Kalzan) + 20 cc. cod liver oil daily	Ca:	0,2596	1,6117	0,2233	2,0946	+0,3854
			P:	1,0734	0,8233	0,1190	2,0157	+0,1734
			Mg:	0,0960	0,3050	0,0230	0,4240	+0,1159
3	1	Ordinary	Ca:	0,0264	1,1292	0,1520	1,3076	÷-0,2209
			P:	0,6483	0,8550	0,0660	1,5693	÷-0,0179
			Mg:	0,0601	0,2975	0,0152	0,3727	+0,0824
3	1 1/2	Ordinary + 1 liter milk daily	Ca:	0,0402	1,4067	0,1693	1,6162	+0,1524
			P:	0,6333	0,6317	0,0733	1,3383	÷-0,0753
			Mg:	0,0067	0,2650	0,0169	0,2886	+0,1638
3	2	As above + 20 cc. cod liver oil daily	Ca:	0,0560	1,7133	0,1467	1,9160	÷-0,0573
			P:	1,0467	0,6210	0,0637	1,7314	÷-0,3287
			Mg:	0,1057	0,2040	0,0147	0,3244	+0,1426

3	2 1/2	As above	Ca:	1,7686	0,0563	1,8767	0,2127	2,1457	÷ 0,3771
			P:	1,3650	1,0566	0,6417	0,0923	1,7906	÷ 0,8956
			Mg:	0,4524	0,0760	0,2533	0,0213	0,3506	+ 0,1018
3	5 1/2	As above + 0,546 gm. Ca (Kulzan) daily	Ca:	2,3500	0,0532	1,5050	0,0920	1,6502	+ 0,6998
			P:	1,9728	0,8466	0,7900	0,0710	1,7076	+ 0,2652
			Mg:	0,4958	0,0103	0,2850	0,0150	0,3103	+ 0,1255
5	3/4	Ordinary	Ca:	1,3408	0,0993	0,7125	0,1825	0,9343	+ 0,4065
			P:	1,4723	0,5762	0,7200	0,0735	1,3697	+ 0,1026
			Mg:	0,3566	0,0299	0,0654	0,0182	0,1135	+ 0,2481
7	1 1/2	Ordinary	Ca:	1,7013	0,3732	0,8650	0,2600	1,4982	+ 0,2031
			P:	1,7762	0,3630	0,4550	0,0815	0,8995	+ 0,8767
			Mg:	0,3963	0,0847	0,1538	0,0260	0,2145	+ 0,1818
8	3/4	Ordinary	Ca:	1,1806	0,0113	0,4975	0,2280	0,6768	+ 0,5128
			P:	1,2834	0,2875	0,1975	0,1430	0,6280	+ 0,6554
			Mg:	0,2708	0,0238	0,0547	0,0215	0,1000	+ 0,1708
14	1	Ordinary	Ca:	1,7730	0,0716	1,0925	0,1857	1,2857	+ 0,4873
			P:	1,5330	0,9850	0,5369	0,0874	1,5493	÷ 0,0163
			Mg:	0,3370	0,0436	0,0689	0,0222	0,1347	+ 0,2023

In case no. 5 it is seen in the 6th experiment that an addition of cod liver oil to the usual diet did not change the negative balance. When the woman took an extra amount of milk increasing the calcium intake from 0,8460 to 1,4808 gr. daily in the 7th experiment the Ca balance was considerably improved. The P balance remained practically unchanged.

In case no. 7 we see that addition of cod liver oil in the 2nd experiment improved the negative Ca balance considerably bringing the Ca loss to the half amount of what it was before. A good effect was also noticed on the P balance. In the next experiment when a quart of milk was taken, the balance became nearly positive for Ca and positive for P.

We have also used the artificial D vitamin in form of *Vigantol*. This addition seemed to be of value in some cases. For inst. in the 4th experiment on woman no. 13. An improvement of the balance was found, but it was not able to bring the Ca balance over to a positive one counting the fetus.

From the 3 women no. 15, 16 and 17 we may follow the result of »*Vigantol*» addition on an otherwise completely unchanged Ca intake. In woman no. 15 we find the balance before and after administration of *Vigantol* nearly unchanged. In the woman 16 and especially in no. 17 a good improvement is noticed but the Ca balance in no. 16 and the P balance in no. 17 are remaining negative. The P intake in no. 17 is however very low.

Neither in the lactation period cod liver oil seems to have any dominating effect on the balance as will be seen from table 6, p. 30. In the 2nd experiment on the lactating woman no. 1 we find that an extra addition of 1 liter milk turned the Ca and P balance to a good positive one. In the 3rd experiment addition of cod liver oil did not have any positive effect. (Unfortunately Kalzan was also given at the same time by a mistake). In case no. 3 the Ca and P balance did not become positive untill the Ca and P intake had been raised to a considerable amount in spite of the addition of cod liver oil.

If we consider the influence of vitamin D addition on

the excretion of Ca through urine and feces, we find that of 6 double experiments where the Ca intake was kept constant before and after vitamin addition the excretion of Ca in urine increased just in 2 experiments, woman no. 11 and 13 (see table 5). In the 4 other experiments, woman no. 3, 15, 16 and 17 (see table 5), the excretion of Ca decreased. In 5 experiments, woman no. 11, 13, 15, 16 and 17, the excretion of Ca in feces has decreased after addition of vitamin. In the 6th experiment of woman no. 3 the fecal excretion was very slightly increased.

It is however a question whether or not we are allowed to draw any conclusion from this slight lowering of the fecal Ca. When the urinary Ca is unchanged or even decreased the lowering of Ca in feces does not exactly point to an increased utilization of Ca in the organism as the fecal Ca is partly excreted and partly unabsorbed Ca.

We find that addition of vitamin D to the diet in a few cases improved the balance. In the majority of cases however, it did not have any distinct effect on the Ca and P balance in pregnancy. It is evident from the experiments presented above that it is the intake of Ca and P which is the dominating factor in the balance. When the Ca intake is brought up to the level of 1,6 gm. daily or above, a positive balance is usually the result. Nevertheless, the diet of these women have to be characterized as one low in vitamins, particularly in D vitamin.

As far as we now can deduct from our experiments concerning the problem of the negative Ca and P balance in pregnancy, the daily Ca and P intake must not fall below a certain level: 1,6—1,7 gm. Ca and about 2,0 gm. P pr. day. An addition of vitamin D when the Ca and P intake is below this level does not seem to be able to bring the balance up to a positive one. When the balance is negative even on an intake above this level a vitamin addition is evidently of significance. That is to say: *a certain amount of Ca and P in the diet is necessary during the last part of pregnancy in*

order to get a positive Ca and P balance, and this amount is higher than usually recognized.

As stated before many other factors have to be paid attention to in making up an ideal diet for pregnant women. The diet must contain a sufficient amount of all vitamins with a certain relationship between Ca and P. The diet must contain a surplus of base, according to SHOHL (49) pregnancy and lactation require additional alkali, a minimum of 150 cc. 0,1 N base pr day, to give the best conditions for a good retention of the calcifying minerals. The diet must furthermore contain ruffage in order to regulate the bowels, must be palatable and easily digestible.

From august 1930 the diet in the home has been changed according to the principles stated above. This diet has a caloric value of about 3000 cal. containing 90 gm. protein, 1,6—2,0 gm. Ca, 1,8—2,0 gm. of P and 0,4 gm. of Mg daily with an excess of base varying around 15—30 cc. of 1 N base according to SHERMAN and GETTLER's analyses of food.¹ The relation of Ca:P has an average value of 0,9. In the dark season 10 cc. of cod liver oil has also been given when not refused. The first results from 4 experiments on 4 women may be seen from table 7 p. 35. The balance counting fetus is still negative.

By examining the list of diet of these 4 women it was found, however, that they had just taken a minimum amount of the fruit and vegetables ordered.

When the fruit and vegetables were increased, we may see from table 8 p. 36 that all 9 experiments performed on 9 different women are positive whether cod liver oil is added to the diet or not. As many women are easily enausiated by taking cod liver oil, particularly during pregnancy, and often refuse it, it was of great practical importance to find out whether or not it is possible to get a positive balance whitout such an addition.

As we may see from table 8 all 5 experiments performed

¹ Journ. Biol. Chem. 1912 XI, 323.

Table 7. Metabolism Studies on Regulated Diet.

Woman no.	Month of pregn.	Diet	Minerals studied gm.	Intake	O u t p u t			Balance	
					Urine	Feces	Total	Without count. fet.	Count. fet.
18	8 1/2	Regulated diet	Ca:	1,765	0,125	1,387	1,462	+ 0,303	- 0,153
			P:	1,509	0,712	0,507	1,219	+ 0,290	+ 0,086
			Mg:	0,336	0,210	0,136	0,336	+ 0,000	- 0,009
19	7	Regulated diet	Ca:	1,540	0,255	1,250	1,505	+ 0,065	- 0,421
			P:	1,493	0,640	0,525	1,165	+ 0,328	+ 0,074
			Mg:	0,313	0,029	0,132	0,161	+ 0,152	+ 0,143
20	8	Regulated diet	Ca:	1,736	0,121	1,570	1,691	+ 0,040	- 0,411
			P:	1,714	0,675	0,840	1,515	+ 0,199	- 0,065
			Mg:	0,367	0,035	0,114	0,149	+ 0,218	+ 0,209
21	8	Regulated diet	Ca:	1,739	0,295	1,337	1,632	+ 0,107	- 0,349
			P:	1,701	0,750	0,425	1,175	+ 0,526	+ 0,272
			Mg:	0,340	0,010	0,201	0,241	+ 0,099	+ 0,090

Table 8. Metabolism Studies on Regulated Diet with Addition of Cod Liver Oil or Eggs.

Woman no.	Month of pregn.	Diet	Minerals studied gm.	Intake	O u t p u t			Balance	
					Urine	Feces	Total	Without count. fet.	Count. fet.
22	7 1/2	Regulated diet + 10 cc. of cod liver oil daily	Ca:	1,706	0,490	0,985	1,175	+ 0,531	+ 0,075
			P:	2,080	1,350	0,530	1,880	+ 0,200	- 0,055
			Mg:	0,383	0,108	0,238	0,346	+ 0,017	+ 0,008
23	8	Regulated diet + 10 cc. of cod liver oil daily	Ca:	1,562	0,307	0,763	1,070	+ 0,492	+ 0,096
			P:	1,735	0,735	0,700	1,435	+ 0,300	+ 0,046
			Mg:	0,386	0,083	0,150	0,213	+ 0,173	+ 0,164
24	7	Regulated diet + 10 cc. of cod liver oil daily	Ca:	1,646	0,240	0,950	1,190	+ 0,456	0,000
			P:	1,896	0,522	0,422	0,944	+ 0,892	+ 0,638
			Mg:	0,461	0,050	0,120	0,170	+ 0,291	+ 0,300
25	8 1/2	Regulated diet	Ca:	1,625	0,147	0,840	0,987	+ 0,638	+ 0,182
			P:	1,843	0,580	0,362	0,942	+ 0,901	+ 0,647
			Mg:	0,392	0,018	0,121	0,139	+ 0,253	+ 0,244
26	8 3/4	Regulated diet	Ca:	1,711	0,067	0,880	0,947	+ 0,764	+ 0,308
			P:	1,966	0,310	0,520	0,830	+ 1,136	+ 0,882
			Mg:	0,331	0,030	0,079	0,109	+ 0,322	+ 0,313

27	8	Regulated diet	Ca:	1,827	0,207	1,117	1,324	+ 0,503	+ 0,047
			P:	1,923	0,450	0,632	1,082	+ 0,241	+ 0,527
			Mg:	0,431	0,036	0,122	0,158	+ 0,273	+ 0,264
28	8	Regulated diet	Ca:	2,157	0,084	1,475	1,559	+ 0,508	+ 0,112
			P:	2,032	0,642	0,715	1,337	+ 0,675	+ 0,421
			Mg:	0,380	0,107	0,242	0,349	+ 0,031	+ 0,022
29	8	Regulated diet	Ca:	2,090	0,101	1,218	1,319	+ 0,771	+ 0,315
			P:	2,163	0,533	0,698	1,231	+ 0,982	+ 0,678
			Mg:	0,504	0,044	0,241	0,285	+ 0,219	+ 0,210
30	8	Regulated diet	Ca:	1,948	0,116	0,937	1,053	+ 0,805	+ 0,489
			P:	1,684	0,800	0,452	1,252	+ 0,382	+ 0,123
			Mg:	0,369	0,095	0,159	0,254	+ 0,115	+ 0,106

For the last 6 women 1 egg daily added to the diet.

Diet list. Example of a Diet during a 4 Days Metabolism Period.

Meals	1st day	2nd day	3rd day	4th day
Breakfast:	Whole wheat bread 70 gm.	57 gm.	67 gm.	105 gm.
	Butter 15 "	17 "	15 "	12 "
	Cheese 19 "	0 "	17 "	23 "
	Apples 97 "	90 "	96 "	68 "
	Carrots 50 "	47 "	60 "	65 "
Forenoon:	Milk 300 "	300 "	300 "	300 "
	Oats } Oatmeal 20 gm.	20 gm.	20 gm.	20 gm.
	Milk } 200 "	200 "	200 "	100 "
	Whole wheat bread 12 "	123 "	135 "	91 "
	Butter 20 "	24 "	22 "	22 "
Dinner:	Cheese 15 "	35 "	16 "	20 "
	Carrots } 100 gm.	Milk } Fish- 100 gm.	Tomato } 68 gm.	Rice } 21 gm.
	Cabbage } 93 "	Wheat flour } 15 "	Wheat flour } 20 "	Cream } 350 "
	Fish 184 "	Meat 70 "	Butter 55 "	Milk } of rice 145 "
	Potatoes 170 "	Carrots 57 "	Fish 112 "	Meat 10 "
Afternoon:	Butter 20 "	Cabbage 130 "	Carrots 79 "	Wheat flour 10 "
	Whole wheat bread 115 gm.	Potatoes 113 "	—	Beans 55 "
	Milk 200 "	—	—	Potatoes 119 "
	Butter 25 "	—	—	—
	Oranges 200 "	—	—	—
Supper:	Cheese 1 "	105 gm.	60 gm.	150 gm.
	Egg 1	200 "	100 "	—
	Whole wheat bread 85 gm.	—	—	—
	Butter 15 "	15 "	15 "	30 "
	Milk 300 "	199 "	100 "	400 "
	Tomato 14 "	—	—	30 "
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without addition of cod liver oil are positive. 1 egg is included in the diet of these women.

An example of the regulated diet given during such a 4 days metabolism study is recorded below on p. 38.

Thus we find that a positive balance may be established in pregnancy in the majority of cases, even in the last part when the Ca need is highest. We have to mention that our material consists just of primiparae as no multiparae are allowed to enter the home.

It may be more difficult to establish a positive balance in cases of multiparae what may be thought of when studying the experiments performed by Macy and Hunscher showing a marked Ca loss even on a Ca intake above 2,0 gm. pr. day.

In a later paper, however, the same authors have achieved an improvement in the Ca balance during lactation by adding vitamin B and D, pointing to the lack of such factors in the diet.

Table 9. The Ca-, P- and Mg-Content of Human Milk.

Woman no.	On ordinary diet.			After 1 week's intake of 0,546 gr. Ca pr. day. ("Kälzan")		
	Pct. Ca	Pct. P	Pct. Mg	Pct. Ca	Pct. P	Pct. Mg
1	0,0177	0,0067	0,0022	0,0213 (+)	0,0038 (÷)	0,0023 (+)
2	0,0256	0,0133	0,0031	0,0307 (+)	0,0122 (÷)	0,0026 (÷)
3	0,0314	0,0123	0,0032	0,0375 (+)	0,0125 (÷)	0,0024 (÷)
4	0,0288	0,0119	0,0029			
5	0,0298	0,0157	0,0039	0,0417 (+)	0,0147 (÷)	0,0029 (÷)
6	0,0254	0,0126	0,0029	0,0347 (+)	0,0147 (+)	0,0029 (=)
7	0,0268	0,0142	0,0035	0,0337 (+)	0,0123 (÷)	0,0032 (÷)
8	0,0234	0,0118	0,0030	0,0297 (+)	0,0125 (+)	0,0032 (+)
9	0,0233	0,0140	0,0039			
10	0,0278	0,0125	0,0035	0,0284 (+)	0,0137 (+)	0,0026 (÷)
11	0,0258	0,0158	0,0034	0,0298 (+)	0,0152 (÷)	0,0029 (÷)
12	0,0288	0,0146	0,0033	0,0353 (+)	0,0128 (÷)	0,0023 (÷)
13	0,0299	0,0152	0,0034	0,0370 (+)	0,0135 (÷)	0,0030 (÷)
14	0,0256	0,0134	0,0035	0,0390 (+)	0,0144 (+)	0,0037 (+)

A similar factor may play a rôle in their earlier experiments. We have to consider a pregnancy period in a woman's life a quite normal event which should not be accompanied by excessive loss of significant constituents of the body. If the diet is composed as to meet all demands, a positive balance of Ca and P should be expected even in multiparae.

A negative Ca balance during pregnancy and lactation may also affect the composition of the mother's milk as we may see from table 9, p. 39. The Ca and P content of the breast milk of 14 women staying in the home and living on the same unregulated diet as the other women examined was below what is considered as an average value according to COURTNEY (50) namely: 33 mgm. % of Ca, 15 mgm. % of P and 5 mgm. % of Mg.

It is evident from the same table that the Ca content of the milk may be brought up to a higher Ca value after increased Ca intake in form of a calcium lactate preparation, (Kalzan). The values of P and Mg are unchanged or even lower than before. It has been demonstrated quite frequent on cows and goats that the Ca and P content of milk may vary considerably according to the diet given to them. There are just few analyses in this respect on women. COURTNEY (50) however has plainly shown that women on a deficient diet as far as calories, organic and inorganic components are concerned, secrete a milk with a content of mineral salts, among others, Ca, below what she considers as an average value: 0,033 %.

C. Comment.

It is evident from these experiments that women eating freely of a diet quite commonly used in Norway as a rule show a negative Ca and P balance during the last months of pregnancy. The Ca loss pr. day amounted sometimes to 0,5 gm. As a similar diet low in Ca and P is commonly used also in other countries, as for instance in America according to the investigations earlier mentioned, we may consider such a Ca

and P loss being of quite common occurrence in pregnant women.

Three questions then naturally arise:

How is such a Ca loss possible? What effect may it have on the mother? What effect may it have on the fetus?

As to the first question the recent investigations of BAUER, AUB and ALBRIGHT (51) have given a fairly good answer. They have found that bone trabeculae are easily depleted by long continued negative calcium balance. In this respect the bone trabeculae serve as the storehouse of readily available calcium. The »shafts» have a slow progressive exchange of inorganic salts and are not influenced except in cases of unusual body demand.

A long continued high calcium diet results in a rapid accumulation of the trabeculae.

The second question: what effect such a negative balance may have on the mother, will mostly depend on her store of Ca previous to the pregnancy, and how much the Ca loss may amount to during the pregnancy. If the pregnancy is followed by a long lactation period, the diet during this period has to be considered as well.

Is the store of Ca low in her organism before a pregnancy starts, and the diet during pregnancy low in Ca and P and vitamins, it is natural, according to this conception of the Ca metabolism, to ascribe many of the pathological conditions occurring during pregnancy to this calcium loss. Of these conditions we will mention dental caries of quite common occurrence during and following pregnancy, and the above mentioned finding of low blood Ca and low salivary Ca during the last part of pregnancy. As mentioned before Vignes has ascribed osteomalacia, latent tetany, vomiting and eclampsia to such a disturbance in the Ca and P metabolism. From the second part of this paper: Experiments on dogs, we will demonstrate some of the conditions which may develop in the mother-animal as a result of a negative Ca balance.

As far as the third question is concerned: what effect, if any, such a negative Ca and P balance may extend to the

fetus, there are two points in which we are particularly interested: If any change may be noticed in the newborn infant. Secondly: if pathological conditions in the hard tissues of the organism, occurring later in life, mostly as the two diseases: dental caries and rickets, may be influenced by this negative Ca balance during pregnancy. In other words, if the predisposition to these diseases is laid down during such conditions.

As mentioned above the calcification of the deciduous teeth starts at the 17th week of fetal life, and is going on throughout the whole fetal period. The calcification of the first permanent molar starts during the last part of this period and of the permanent incisors during the first year of life (see fig. 1 and 2, p. 12 and 13).

We consider it very probable that the metabolism process going on in the mother organism during the tooth formation and calcification are of great significance for the resistance to caries later in life, and in the last part of this work we will discuss this more thoroughly.

As far as rickets is concerned we know that the ossification of the bones goes on rather rapidly from the middle of the fetal life and as we see from table 3 and 4 (p. 18) the two very last months are the most significant just for Ca and P deposition. This is the very period examined in this work.

It is very difficult if not practically impossible on a clinical material to study in details the effect of such a disturbance in the Ca and P metabolism on the child. If the newborn infant is examined according to our usual clinical methods no rickets has been found as earlier investigations show. As mentioned before Yllpö and Hess occasionally have found some roentgenological evidence of rickets incipiens in newborn infants. It is however considered of very rare occurrence. Compare later our own findings on newborn infants.

Even with such negative findings in the newborn, changes may have occurred in the composition of the fetal organism which may dispose to the development of these conditions in the postnatal life. Such changes may only be detected by experi-

ments on animals where the material is to our full disposal. In the next part of this thesis we will present the result of such experiments.

Furthermore we know that the postnatal care of the infant, particularly during the first year, but also (especially for dental caries) during later years as well, plays the most important rôle in the development of these two diseases. By ideal feeding during the infant's first year possible existing pathological conditions from fetal life may be repaired with one exception at least: The hypoplasia of the teeth. An other important point has to be considered, namely acute and chronic infections of the child during this time. These may influence the appetite directly or indirectly, the metabolism and the whole nutritional state of the child. We have further to remember the domestication, the local and general hygiene, and particularly the influence of sunshine as very important factors in this connection.

In order to study the influence of the prenatal factors under fully controlled postnatal conditions, we have tried to reproduce in dogs the negative Ca and P balance as found in the women. In this way we will be able to study in details the effect of such changes on the mother and particularly on the offspring.

IV. Investigations on the Mineral Metabolism of Dogs during Gestation and Lactation with a Special Study of the Offspring.

The purpose of these investigations on dogs was to study the changes which eventually may occur in the mother and youngs when the mother during gestation is kept on a diet mainly corresponding to the diet taken by the women described in the first part of this paper.

The diet may be characterized as poor in calcium and phosphorus, and low in vitamins A and D.

A. Short Survey of Previous Literature.

In the literature we find several investigations of similar nature described, but none of them cover exactly our plan. Besides the earlier mentioned publications in this connection (see p. 8 and 9) we want to remind of DIBBELT's experiments on dogs (52) from 1910. He fed a dog a calcium poor diet throughout its whole gestation period. He calculated that the mother had lost 4,22 gm. Ca as result of the gestation. In the lactation period too a calcium loss was found resulting in a lowering of the calcium content of the dog's milk to the half of its normal value. This Ca starvation resulted in thickened osteoid zones and large lacunae of resorption in the ribs. Any chemical analysis of the bones was not performed. In the earlier mentioned work by KORENCHEVSKY and CAR (13) large histopathological changes as well as chemical changes were noticed in the bones of young rats the mothers of which were given a ration low in Ca, vitamin A and D.

During 1930 M. JONES (53) has published some experiments on bitches similar to ours just that the diet was low in all vitamins besides being low in Ca and P. She found a marked effect on the dental condition of brood bitches and upon the dental and skeletal development of their offspring.

B. Own Investigations on Dogs.

1. Mineral and Vitamin Deficiency.

A 1 year old bitch was given a ration low in Ca, P and vitamins A and D, consisting of wheat, ryeflour and cocofat cooked to a gruel, to this added powder of skimmed milk, raw horsemeat, NaCl, Fe, marmit and lemon or orange juice. The daily ration consisted of:

meat	50 gm.
milkpowder	10 »
lemonjuice	5 cc.
marmit	5 gm.
NaCl	3 »
Fe	0,1 »
cocofat	10—40 »

wheat and ryeflour from 90—360 gm. (according to the appetite of the dog).

The protein content of the ration: 2—3,5 gm. pr. kg. and the caloric value: 55—80 cal. pr. kg. of body weight should be quite satisfactory according to other investigations. The Ca and P content of the diet calculated pr. kg. body weight was about the same for the dogs as for the women, about 10 mgm. Ca and 16—18 mgm. P, and the Ca: P relation was 0,5—0,7. The dogs were kept in a large room with no free access to direct sunlight. Metabolism studies performed just before the gestation period showed that this ration gave a slightly positive Ca and Mg balance, and a slightly negative P balance, see table 10, p. 46. Ca and P of blood serum were normal.

Before gestation the middle part of one of the metatarsal bones of the right hindlegg was extirpated in narcosis.

Table 10. Metabolism Studies during Gestation of the Dog Lillemor.

(Ca, P, vitamin A and D deficiency.)

Week of gestation	Minerals studied	Intake gm.	Daily Output			Balance gm.	Pr. 100 c.c. serum	
			Urine gm.	Feces gm.	Total gm.		Ca mgm.	P mgm.
Before copulation	Ca:	0,1591	0,0305	0,0943	0,1248	+ 0,0343	11,0	4,63
	P:	0,2885	0,3043	0,0993	0,4036	÷ 0,1201		
	Mg:	0,1030	0,0249	0,0473	0,0722	+ 0,0308		
1	Ca:	0,1591	0,0221	0,1923	0,2144	÷ 0,0553		
	P:	0,2885	0,3470	0,1562	0,5032	÷ 0,2197		
	Mg:	0,1030	0,0509	0,0618	0,1127	÷ 0,0097		
2	Ca:	0,1728	0,0300	0,2217	0,2517	÷ 0,0789		
	P:	0,3310	0,3430	0,2557	0,5987	÷ 0,2677		
	Mg:	0,1413	0,0433	0,1068	0,1501	÷ 0,0088		
3	Ca:	0,1882	0,0291	0,2673	0,2964	÷ 0,1082		
	P:	0,3785	0,3633	0,2567	0,6200	÷ 0,2415		
	Mg:	0,1806	0,0480	0,1190	0,1670	+ 0,0136		
4	Ca:	0,1882	0,0397	0,3023	0,3420	÷ 0,1538	9,25	4,00
	P:	0,3785	0,3504	0,2817	0,6321	÷ 0,2536		
	Mg:	0,1806	0,0480	0,1399	0,1879	÷ 0,0073		
5	Ca:	0,1882	0,0298	0,3672	0,3970	÷ 0,2088	9,85	3,56
	P:	0,3785	0,4203	0,3047	0,7250	÷ 0,3465		
	Mg:	0,1806	0,4907	0,1385	0,1882	÷ 0,0076		
6	Ca:	0,1882	0,0303	0,2527	0,2830	÷ 0,0948	10,07	4,00
	P:	0,3785	0,3433	0,1952	0,5385	÷ 0,1600		
	Mg:	0,1806	0,0466	0,0562	0,1028	+ 0,0778		
7	Ca:	0,1699	0,0138	0,2370	0,2508	÷ 0,0809	9,80	3,64
	P:	0,3152	0,3650	0,3133	0,6783	÷ 0,3631		
	Mg:	0,1295	0,0246	0,0470	0,0716	+ 0,0579		

Week of gestation	Minerals studied	Intake gm.	Daily Output			Balance gm.	Pr. 100 c.c. serum	
			Urine gm.	Feces gm.	Total gm		Ca mgm.	P mgm.
8	Ca:	0,1625	0,0100	0,1332	0,1432	+ 0,0193		
	P:	0,2993	0,2015	0,0920	0,2935	+ 0,0058		
	Mg:	0,1161	0,0307	0,0305	0,0612	+ 0,0549		
9	Ca:	0,1625	0,0115	0,2170	0,2285	÷ 0,0660		
	P:	0,2993	0,2642	0,1605	0,4247	÷ 0,1254	8,40	3,47
	Mg:	0,1161	0,0277	0,1055	0,1382	÷ 0,0171		

Table 11. Metabolism Studies during Lactation of the Dog
Lillemor.
(Ca, P, vitamin A and D deficiency.)

[illegible]

During gestation a 3 days metabolism experiment on Ca, P and Mg was performed every week throughout the whole period. The result is seen from table 10. The Ca as well as the Mg balance changed to a negative one during the 1st week. The 5th week the negative Ca balance reached its maximum, then it decreased and turned positive the 8th week, but became again negative just before delivery. The negative P balance was most marked the 7th week and passed over to the positive side at the 8th week. The last metabolism experiment was again negative. The Mg balance was also often negative.

Serum Ca and P decreased, as we see, and reached the lowest value at the end of gestation.

After the normal gestation period of 9 weeks the bitch gave birth to 4 evidently normal puppies. The one was at once killed for examination while the three others stayed with the mother and suckled. The puppies were for the rest of the time given the same ration as the mother received during gestation and lactation with some necessary modifications mentioned below.

3 weeks after delivery a metabolism experiment was again performed showing over three times as great negative Ca balance as the maximum negative Ca balance during gestation, see table 11, p. 47. The P balance was negative as well, where-as the Mg balance was positive. 1 week later the Ca balance was somewhat less negative while the P balance was more negative.

During the whole gestation period the dog looked normal, not however during the lactating period.

As may be seen, the serum Ca and P had decreased considerably as early as 4 days after birth. 8 days after birth the dog showed manifest symptoms of tetany: dyspnoe, the whole animal was spastic with shivering of the body, the dog was restless. A blood test gave tetanic Ca value: 5,2 mgm. Ca and 2,9 mgm. P. pr. 100 cc. of serum. On account of this tetanic attack the dog was given an injection of 9 cc. of 25 % magnesium sulfate solution and then given 500 cc. of

Table 12. Status of the Dog Lillemor (first Dog) at the End of Gestation and at the End of Lactation.

(Ca, P, vitamin A and D deficiency.)

	Gm. Ca.	Gm. P.	Gm. Mg.
Total intake during gestation	10,5894	20,3825	8,9113
Loss through urine and feces	15,9959	33,8282	7,8065
Loss through 4 fetus	9,4144	5,8096	0,3184
Total loss during gestation	25,4103	39,6378	8,1249
Balance at the end of gestation	÷ 14,8709	÷ 19,2503	+ 0,7864
<hr/>			
Intake through food during lactation . .	7,2944	12,1245	4,1587
Intake through feces from the puppies during lactation	3,9700	2,7300	0,8400
Total intake during lactation	11,2644	14,8545	4,9987
Loss through urine and feces	10,0000	13,2000	2,6400
Loss through secreted milk	30,9000	20,6000	1,4500
Total loss during lactation	40,9000	33,8000	4,0900
Balance at the end of lactation not count- ing gestation	÷ 29,6856	÷ 18,9455	+ 0,9087
Balance at the end of lactation counting gestation	÷ 44,5065	÷ 38,1958	+ 1,6951

milk by gavage. Then the calcium intake was raised first by calcium lactate later by adding more skimmed milk powder to the ration.

The following week the animal revealed a latent tetany with two small tetanic attacks which were checked by magnesium sulfate injections. The serum calcium remained between 5 and 6 mgm. the whole time. The last part of the lactation period the animal's condition improved somewhat but the weight decreased constantly. At the end of the lactation, 6 weeks after birth, the Ca was 8,9 mgm. and P 3,48 mgm. pr. 100 cc.

Table 13. Analyses of Metatarsal Bones from Mother Animals.

	Pct. ash of dry weight	Pct. Ca of		Pct. P of	
		dry weight	ash	dry weight	ash
<i>Lisa.</i>					
(Normal)	64,6	26,2	40,7	11,1	17,0
<i>Lillemor I.</i>					
Before I gestation . . .	64,9	26,2	40,8	11,5	17,7
<i>Lillemor II.</i>					
After I gestation with lac- tation	59,9	23,8	39,2	10,4	17,5
Pct. difference from normal	÷ 7,6	÷ 11,1	÷ 3,2	÷ 8,0	÷ 1,6
<i>Lillemor III.</i>					
After II gestation with lactation	55,3	22,8	41,4	9,9	17,9
Pct. difference from normal	÷ 14,8	÷ 12,9	+ 2,2	÷ 12,8	+ 0,6
<i>Stella I.</i>					
After first lactation . . .	61,6	25,3	40,9	10,8	17,5
Pct. difference from normal	÷ 5,7	÷ 3,4	+ 1,0	÷ 4,4	÷ 1,6
<i>Stella II.</i>					
After second lactation . .	59,9	23,8	40,2	10,5	17,6
Pct. difference from normal	÷ 7,6	÷ 9,2	+ 0,7	÷ 6,6	÷ 0,56

Stella I. Normal diet during pregnancy. Deficient diet during lactation.¹

Stella II. Ca and P deficiency during gestation und lactation.

serum. After lactation both serum Ca and P increased to normal values. 4 months after delivery the serum Ca was 10,10 mgm. and P 3,5 mgm.

We are now going to consider the status of the mineral metabolism of the dog. On table no. 12, p. 49 we find the intake of Ca, P and Mg and the loss of the same constituents through feces and urine exactly calculated.

¹ The same deficiency as for Lillemor. About one year between these two gestation periods.

Table 14. Analyses of Milk from the Mother Animals.

Dog	Diet deficiency	Deficiency started	Days after delivery	Pr 100 gm milk			
				Ca gm	P gm	Mg gm	
<i>Lisa</i> (Normal)	No.		17	0,253	0,181	0,009	
			25	0,271	0,191	0,010	
			30	0,278	0,213	0,009	
<i>Lillemor II</i>	Ca, P, vitamin A & D		Before gestation	17	0,368	0,218	0,016
				25	0,223	0,155	0,010
				30	0,181	0,165	0,011
<i>Stella I</i>	"	At delivery		21	0,285	0,144	0,009
				31	0,227	0,098	0,007
<i>Stella II</i>	Ca & P	Before gestation		17	0,245	0,133	
			25	0,217	0,084	0,007	
			31	0,331	0,165	0,019	

By analysis of one of the newborn puppies killed immediately after birth we calculated the amount of Ca, P and Mg necessary to build up the 4 fetus. As we see the balance at the end of the gestation became highly negative for Ca (14,87 gm.) and for P (19,25 gm.) and faintly positive for Mg.

The mineral intake through the diet was exactly determined during the lactation period. To this must be added the mineral content of the feces of the youngs as the mother always eat the feces. This value was estimated as exactly as possible.

During the lactation period we did not perform metabolism experiments as often as during gestation on account of the poor condition of the animal and particularly on account of difficulties in keeping the mother separated from the youngs. The Ca, P and Mg loss through feces and urine just as well as through the milk (the latter was analysed several times during the period), was calculated as exactly as possible. The

Table 15. Analyses of Femur

	Fresh weight gm.	Dry weight gm.	Pet. dry weight of fresh w.	Pet. ash of fresh w.	Pet. ash of dry w.
<i>Lord.</i>					
(Normal)	1,343	0,4382	32,7	16,9	51,8
1. <i>Paal</i>	1,055	0,3444	32,7	15,1	46,4
Pet. difference from normal			0,0	÷ 10,7	÷ 10,4
2. <i>Fritz</i>	0,964	0,2567	26,6	11,3	42,5
Pet. difference from normal			÷ 18,7	÷ 33,1	÷ 18,0
3. <i>Stegg</i>	1,406	0,3790	27,0	11,7	43,2
Pet. difference from normal			÷ 17,5	÷ 30,8	÷ 16,6

1. Paal's mother during gestation lived on Ca, P, vitamin A & D deficient diet. Paal from I litter.
2. Fritz's mother during gestation lived on Ca, P, vitamin A & D deficient diet. Fritz from II litter. (Same mother.)
3. Stegg's mother during gestation lived on Ca & P deficient diet.

mineral balance for the lactation period as well was negative for Ca and P, twice as great for Ca while about the same for P compared with the negative balance during gestation. The Mg balance was positive,

The total balance for the gestation and the lactation period together amounted to ÷44 gm. Ca, ÷38 gm P and +1,6 gm. Mg. According to HEISS (54) an adult dog contains about 2,4 % Ca of the body weight. If we suppose the same relation to be present in this dog, the loss of Ca should be 12 % of the original value. This corresponds quite well to the result of the chemical analyses of the metatarsal bone as may be seen from table 13, p. 50 showing that the percentage of Ca of dry weight deviates ÷11,1 % from normal after the first reproductive cycle.

What effect may this gestation with the following lactation have had on the dog? As is stated above, the condi-

from Newborn Puppies.

Pct. Ca of			Pct. P of			Pct. Mg. of		
fresh w.	dry w.	ash	fresh w.	dry w.	ash	fresh w.	dry w.	ash
6,4	19,6	38,0	2,9	8,6	17,0	0,11	0,84	0,66
5,4	16,4	36,0	2,6	7,8	16,9	0,09	0,27	0,57
÷ 15,6	÷ 16,8	÷ 5,8	÷ 10,5	÷ 9,4	÷ 0,6	÷ 18,2	÷ 20,6	÷ 13,6
4,1	15,5	36,6	2,0	7,4	17,4	0,08	0,28	0,68
÷ 36,0	÷ 20,9	÷ 3,7	÷ 31,0	÷ 14,0	+ 2,8	÷ 27,2	÷ 17,8	+ 3,0
4,6	17,2	39,8	2,1	7,6	17,6	0,08	0,29	0,67
÷ 28,1	÷ 12,8	+ 4,5	÷ 27,6	÷ 11,6	+ 3,5	÷ 27,2	÷ 14,7	+ 1,5

tion of the bitch was not very good during the lactation period with a regular attack of manifest tetany. The body weight when gestation started was 15 kg. and just before delivery 18 kg. At the end of the lactation period it was just 11 kg. The milk showed a normal value throughout the first half of the lactation: 0,368 % Ca and 0,218 % P and 0,011 % Mg. Towards the end of the lactating period the mineral content of the milk decreased to 0,181 % Ca, and 0,165 % P, see table no. 14, p. 51.

A chemical analysis of one of the metatarsal bones of the left hind leg resected just after the end of the lactating period showed a lower ash, Ca and P content compared with the corresponding bone resected before copulation. This may be seen from table 13, p. 50. Histopathological examinations of the same bones (performed at the Pathological Department of the Norway Dental School by docent dr. Häupl) is in good correspondance with the chemical results, and will be described later, see p. 75.

The next step in this study was to determine what influence, if any, this negative Ca and P balance of the mother

Table 16. Analyses of the Mandible from Newborn Puppies.

	Dry weight gm.	Pct. ash of dry w.	Pct. Ca of		Pct. P of		Pct. Mg of	
			dry w.	ash	dry w.	ash	dry w.	ash
<i>Lord.</i>								
(Normal) . .	0,4857	46,2	18,6	38,8	8,3	17,4	0,31	0,66
1. <i>Paal</i>	0,4455	41,3	14,5	35,9	7,3	18,2	0,26	0,64
Pct. difference from normal .		÷ 10,6	÷ 22,7	÷ 7,5	÷ 12,0	+ 4,4	÷ 16,1	÷ 3,0
2. <i>Fritz</i>	0,3351	41,3	15,5	37,4	7,5	16,2	0,30	0,72
Pct. difference from normal .		÷ 10,6	÷ 16,7	÷ 3,6	÷ 9,8	÷ 7,9	÷ 3,2	+ 9,1
3. <i>Stegg</i>	0,4477	46,2	17,7	38,2	8,0	17,3	0,30	0,64
Pct. difference from normal .		0	÷ 4,8	÷ 7,5	÷ 3,6	÷ 0,6	÷ 3,2	÷ 3,0

1. Paal's mother during gestation lived on Ca, P, vitamin A & D deficient diet. Paal from I litter.
2. Fritz's mother during gestation lived on Ca, P, vitamin A & D deficient diet. Fritz from II litter.
3. Stegg's mother during gestation lived on Ca & P deficient diet.

might have had on the development of the youngs. The 4 puppies seemed at birth to be quite normally developed and by taking Xray pictures of their extremities no difference could be noticed from those of normal puppies. A chemical analysis, however, of one of the newborn puppies, *Paal*, see table 15, p. 52, 16, p. 54, and 17, p. 55, did not show normal figures. From table 15 we will find that the ash as well as the Ca, P and Mg content of the femur are distinctly below the normal figures, represented by *Lord*, a puppy born by a dog given a normal ration throughout gestation. From table 16 we see that the same holds true for the mandible bone. By analyses of the whole animal the result was a similar one what may be seen from table 17. Nearly all figures for Ca, P and Mg in all these 3 tables for *Paal* are distinctly below

Table 17. Analyses of the Whole Body of Newborn Puppies.

	Fresh weight gm.	Dry weight gm.	Pct. dry w. of fresh w.	Pct. Ca of		Pct. P of		Pct. Mg of	
				fresh w.	dry w.	fresh w.	dry w.	fresh w.	dry w.
<i>Lord</i>									
(Normal) . .	403,0	82,647	20,4	0,77	3,77	0,48	2,12	0,08	0,12
1. <i>Paal</i>	381,8	78,079	20,6	0,61	2,99	0,38	1,85	0,02	0,10
Pct. difference from normal			+ 1,0	÷ 20,8	÷ 20,7	÷ 11,6	÷ 12,7	÷ 16,0	÷ 17,7
2. <i>Fritz</i>	310,0	62,288	21,1	0,56	2,64	0,39	1,88	0,02	0,11
Pct. difference from normal			+ 3,8	÷ 27,8	÷ 30,0	÷ 9,8	÷ 11,8	÷ 8,0	÷ 10,5
3. <i>Stegg</i>	413,0	82,258	19,6	0,67	3,35	0,41	2,04	0,08	0,12
Pct. difference from normal			÷ 3,9	÷ 13,8	÷ 11,2	÷ 4,6	÷ 3,8	0	0

1. Ca, P, vitamin A and D deficiency. First litter.

2. Ca, P, vitamin A and D deficiency. Second litter. Same mother.

3. Ca and P deficiency.

those of the normal puppy Lord. Thus we see that considerable changes in the composition of the bones of newborn puppies may be demonstrated by chemical methods in spite of clinical as well as roentgenological examinations being wholly negative. This abnormality of the bony system, the only one detected, must evidently have increased these animals' disposition to rickets as they developed symptoms of this disease very early and severely, see below.

Throughout the whole nursing period the three remaining puppies developed quite normally except that the body weight was somewhat subnormal. After 5 weeks of lactation the youngs were given the same ration as the mother, and 1 week after weaning the general condition of the youngs was less satisfactory.

On fig. 3 this litter is represented by *Eva* and we find here that the first examination of the blood, performed 45 days after birth, showed a distinct lowering of P from normal, and 50 days after birth a beginning ricketic process was diagnosed by Xrays, 5 days later clinical symptoms of rickets were present. From the same plate we see when similar symptoms were first noticed in a puppy: *Grete*, born and nursed by a bitch, *Stella*, given a normal diet throughout gestation but the above mentioned ration low in Ca, P, vitamin A and D just after delivery. After the end of lactation period the last mentioned puppy, *Grete*, was given the same experimental diet as the first one on the plate, *Eva*. The third curve represents a puppy, *Siss*, born and nursed by a mother on normal diet throughout gestation and lactation and then given the experimental ration.

This plate plainly demonstrates the influence of the diet during gestation and lactation on the time of development of ricketic symptoms in the youngs.

When the diet during the gestation as well as during lactation period of the mother was deficient, the clinical symptoms of rickets in the puppy *Eva* were first observed 55 days after birth. When the diet of the mother animal was normal during gestation, but deficient during lactation, the clinical ricketic symptoms of the puppy *Grete*, did not appear till the 75th day after birth. The last puppy, *Siss*, which had a normal fetal and lactation period, but afterwards was given the experimental ration did not develop ricketic symptoms till the 91st day of life.

85 days old the general condition of the three puppies born by the experimental dog Lillemor, was so poor that cod liver oil had to be given in addition to the usual ration. (The dose was adapted according to the least therapeutic dose for rats under otherwise normal conditions). The blood analyses showed the lowest value 6,1 mgm. Ca and 3,8 mgm. P at this time (the normal value for this age is 10—11 mgm. Ca and 7—8 mgm. P).

Table 18. Analyses of Radius

Name of puppy	Diet deficiency of			Fresh. w. gm.	Dry w. gm.	Pet. dry w. of fresh w.
	mother during		puppy after lact. period.			
	gestation	lactation				
<i>Lisken.</i>						
Normal	No	No	No	9,733	4,709	48,5
<i>Siss</i>	No	No	Ca, P and vitamin A & D	14,150	5,445	38,3
Pet. difference from normal						÷ 21,0
<i>Grete</i>	No	Ca, P and vitamin A & D	— — —	14,010	3,960	28,3
Pet. difference from normal						÷ 41,6
<i>Eva</i>	Ca, P and vitamin A & D	— — —	— — —	8,780	2,077	23,7
Pet. difference from normal						÷ 51,1
<i>Bob</i>	Ca and P	Ca and P	Ca and P	9,940	4,320	43,5
Pet. difference from normal						÷ 10,3
<i>Tell</i>	— — —	— — —	— — —	13,200	4,695	35,6
Pet. difference from normal						÷ 26,6

112 days old the one puppy, Eva, born by Lillemor, died. A chemical analysis of the radius of this puppy was performed. For comparison analyses were performed of the corresponding radius from other puppies of the same age where the deficient diet had started at different periods of the puppie's life. The result of these analyses may be seen from table 18, p. 58. Lisken represents here a normal puppy and serves as control. It is born by a dog given a normal diet throughout gestation and lactation and after weaning the puppy was also kept on a normal diet.

When the Ca, P, vitamin A and D deficiency starts at

from 112 Days Old Puppies.

Pct. ash of		Pct. Ca of			Pct. P of			Pct. Mg of		
fresh w.	dry w.	fresh w.	dry w.	ash	fresh w.	dry w.	ash	fresh w.	dry w.	ash
22,5	46,4	8,9	18,0	39,3	4,0	8,2	17,7	0,15	0,31	0,68
15,6	40,7	6,2	16,1	39,5	2,5	6,6	16,2	0,08	0,20	0,49
÷ 30,7	÷ 12,3	÷ 30,2	÷ 10,6	+ 0,5	÷ 37,5	÷ 19,5	÷ 8,5	÷ 46,7	÷ 35,4	÷ 27,9
8,9	31,3	3,2	11,2	35,7	1,39	5,0	15,7	0,04	0,15	0,48
÷ 61,2	÷ 32,5	÷ 64,1	÷ 37,8	÷ 9,2	÷ 65,3	÷ 39,0	÷ 11,3	÷ 73,3	÷ 51,6	÷ 29,4
5,6	23,3	1,9	8,1	34,9	0,95	4,0	17,2	0,08	0,14	0,59
÷ 75,1	÷ 49,8	÷ 78,7	÷ 55,0	÷ 11,2	÷ 73,3	÷ 51,2	÷ 2,8	÷ 80,0	÷ 54,8	÷ 13,2
9,1	21,0	3,8	8,7	41,0	1,6	3,6	17,4	0,06	0,13	0,61
÷ 60,0	÷ 54,7	÷ 57,6	÷ 52,0	+ 4,3	÷ 60,0	÷ 56,1	÷ 1,7	÷ 60,0	÷ 58,1	÷ 10,3
12,1	34,3	4,8	13,4	39,1	2,0	5,6	16,3	0,06	0,13	0,53
÷ 46,2	÷ 26,1	÷ 46,1	÷ 25,6	÷ 0,5	÷ 50,0	÷ 31,7	÷ 7,9	÷ 60,0	÷ 42,0	÷ 22,0

the end of the lactation period, as for Siss, we will find all values for dry weight, ash, Ca, P and Mg considerably below the normal figures. The lowering is more marked for the puppy Grete, which also had a deficient lactation period. (The mother was just after delivery given the deficient diet). The greatest deviation from normal was found in the radius from the puppy Eva, where the deficient diet had lasted throughout the fetal period in addition, (mother: Lillemor). For this puppy we will find a percentage deviation from normal up to 80.

As we see from this table (18) the bone analyses, go in the same direction as the weightcurves, the blood analyses,

the Xray examinations and the clinical findings of the puppies demonstrated on figure 3, page 56. It corresponds furthermore very well to Xray pictures of radius and ulna from the above mentioned 4 puppies taken 112 days after birth. This may be seen on fig. 4, plate I.

The result of the roentgenological examinations of the mandible showing the developmental stage of the permanent teeth goes also parallel with the above mentioned findings. Fig. 5 a and b plate II will demonstrate this. We find here a very distinct difference in the development of the permanent teeth from the 4 puppies Eva, Grete, Siss and Liskén. The tooth which best illustrates this is the 1st permanent mandibular molar (the Carnassial) which is found to the right on the 4 different pictures. The thickness of the enamel-dentin cap on the top of the mesio-buccal cusp of this tooth is measured and the figures for the respective dogs in succession as above mentioned are: 1,5—2,0—2,3—2,5 mm. If we examine the deciduous teeth very closely we will detect that the root walls of the teeth from Eva is much thinner than is the case from the other puppies.

The difference in the developmental stage of the permanent teeth is even better demonstrated in fig. 6 plate III showing a roentgenogram of the second mandibular incisor carefully dissected out of the jaw from the different puppies. Xrays of the temporary mandibular canine tooth also reveals similar steps in calcification, see fig. 7, plate III.

Chemical analyses of a mandibular temporary canine tooth from the same puppies also illustrate the difference in calcification. As we see from table 19, p. 61 the result of these analyses does not entirely follow that from the radius of the same dogs. We find for instance that the tooth analysis of the dog Grete shows the worst result instead of what we have seen earlier: the dog Eva. At first sight this must seem somewhat surprising but comparing the chemical analyses with the roentgenograms of the same teeth (fig. 7, plate III) a reasonable interpretation of this discrepancy will be found. From the Xrays we see that it is formed much less of the root of Eva's

Table 19. Chemical Analyses of the Mandibular Temporary Canine Tooth from 112 Days Old Puppies.

Name of puppy	Diet deficiency of			Dry weight gm.	Pet. ash of dry weight	Pet. Ca of		Pet. P of	
	mother during		puppy after lact. period.			dry weight	ash	dry weight	ash
	gestation	lactation							
<i>Lisken.</i>									
Normal	No	No	No	0,1445	70,3	25,5	36,3	13,0	18,5
<i>Grete</i>	No	Ca, P and vitamin A & D	— — —	0,1461	62,3	22,2	35,3	11,6	18,4
Pet. difference from normal					÷ 10,7	÷ 13,0	÷ 2,8	÷ 10,7	÷ 0,5
<i>Eva</i>	Ca, P and vitamin A & D	— — —	— — —	0,1353	67,7	24,8	36,7	12,6	18,7
Pet. difference from normal					÷ 3,7	÷ 2,8	+ 1,1	÷ 3,1	+ 1,1
<i>Tell</i>	Ca and P	Ca and P	Ca and P	0,1629	69,0	25,2	36,5	12,8	18,6
Pet. difference from normal					÷ 1,8	÷ 1,2	+ 0,6	÷ 1,6	+ 0,5

tooth than is the case with Grete's tooth. The crowns, however, of these two teeth do not differ particularly. The relation of the crown to the root therefore is not the same in these two cases, and as the enamel (only in the crown) is much richer in mineral substances than the dentin and the cementum (the two hard substances in the root) we will find, when we analyse the crown and the root together, higher figures for inorganic substances in that case where the ratio crown: root is the highest. (The periodontal membrane as well as the pulp was removed before the chemical analysis was performed). The tooth from the normal dog Lisken, neither, represents exactly the correct proportion between crown and root as a part of the tip of the crown was worn off. The figures in the table, therefore, would perhaps have been somewhat higher if this had not been the case. The canine teeth from the other dogs did not show any sign of attrition.

Ground specimens of the deciduous as well as of the permanent teeth from the same puppies show similar relationship as did the other test methods just described, that is: the puppy Eva which has had the longest deficiency period also showed the poorest calcification. The enamel of a permanent incisor from Eva revealed in polarized light to be negative double refracting whereas that from the control puppy Lisken was positive double refracting which is the normal. This as well shows the impairment of the teeth from the defectively fed puppies.

The histological examinations of the radius, ribs, mandible and the teeth demonstrate very plainly that also the histopathological picture may be graded exactly according to the duration of the diet deficiency.

The two remaining puppies of Lillemor, *Per* and *Sonja*, were given cod liver oil from the 85th day after birth in order to keep them alive, as above mentioned for Eva. (The dose was adapted according to the body weight in such a way that it should correspond to the least effective therapeutic dose under otherwise good conditions). The condition of the puppies improved somewhat during the treatment with cod liver oil,

but not very much on account of the low Ca and P intake. From fig. 8, below, the poor condition of one of the puppies, Per, 3 1/2 months old may be seen. The dog was not able to stand alone when this picture was taken, but had to be held up on its feet. On the same picture we see another puppy, *Bitten*, (in the middle) of the same age, given the experimental diet from the end of the lactation period, (from

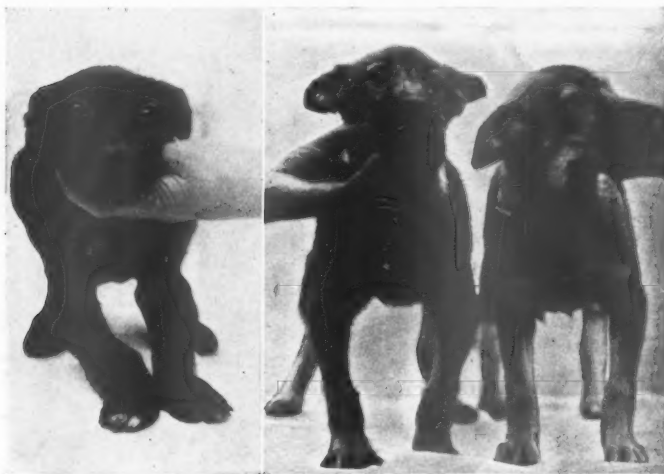


Fig. 8. The picture demonstrates the 3 1/2 months old puppies: Per to the left (deficient diet during fetal life, lactation and afterwards), Bitten in the middle (normal diet during fetal life and lactation, deficient diet afterwards) of the same litter and fed in the same way as Siss. To the right is seen Bitten's normally fed sister (control puppy). Notice the marked bowing of the forelegs of Per, which at that time was not able to stand on its toes. The general condition of Per very poor, that of Bitten very good.

the same litter and fed in the same way as Siss represented by the 1st curve on fig. 3). Throughout gestation and the lactating period the mother had been normally fed. We notice on fig. 8, the striking difference in appearance and especially in the condition of the legs of these two dogs. To the right we see a control animal of the same age 3 1/2 months old (Bitten's normally fed sister).

As the condition of the puppies grew worse the dose of cod liver oil was increased twice the minimal dose. Any improvement however was not noticed, neither clinically nor serologically until extra calcium was given, 0,5 gm. Ca lactate pr. day. But even on this ration the general condition of the puppies was sometimes so poor that they often refused food, and had to be given 100—200 cc. milk daily. When they

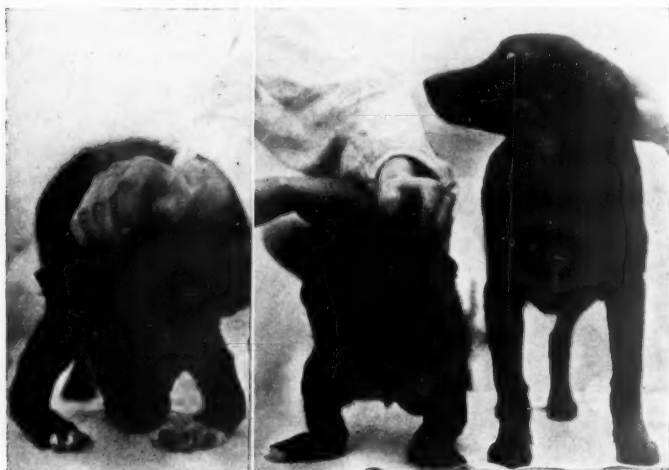


Fig. 9. The picture demonstrates the further development of Per, 7 $\frac{1}{2}$ months old, in the middle and its sister Sonja to the left, both had a deficient diet during fetal life, lactation and afterwards. Both animals had difficulty in walking on account of the bowed legs. To the right is seen a 4 months old control puppy for comparison.

were about 6 months old the blood Ca was 6,2 mgm. and P 3,7 mgm. pr. 100 cc. serum.

Fig. 9, above, shows the condition of Sonja (to the left) and Per (in the middle) both 7 $\frac{1}{2}$ months old. From the bowed legs we may well judge to the severity of the ricketic process. The puppies were not able to stand or walk more than 3—4 minutes at a time. Growth had ceased what is evident when we compare these two puppies with the 4 months old normally fed puppy to the right on the picture.



Fig. 10. The picture demonstrates the further development of Bitten, 7 $\frac{1}{2}$ months old, to the left (normal diet during fetal life and lactation, deficient diet afterwards). The legs are not so bowed as those of the puppies Sonja and Per seen on fig. 9. To the right is seen Bitten's normally fed sister (control) 7 $\frac{1}{2}$ months old.

(This puppy is of the same race). On fig. 10 we see Bitten, 7 $\frac{1}{2}$ months old, born and nursed by a normally fed mother and after weaning given the same diet as the two experimental puppies mentioned above (Per and Sonja). When we compare figs. 9 and 10 we find the condition of Bitten much better than that of Sonja.

The cutting of the permanent teeth of Per and Sonja occurred very late and several of the permanent teeth appeared while the deciduous teeth still were fixed in the jaw. This

led to anomalies in the position of the teeth well demonstrated on fig. 11.

At the age of 9 months the serum Ca and serum P of the two puppies, Sonja and Per, were nearly normal and from this time the general condition of the puppies improved rapidly. One year old they were able to run about, though in a wadling way. Any improvement in the appearance of the legs from what is seen in fig. 9, p. 64 could not be noticed, and the height of the puppies did not increase at all. The

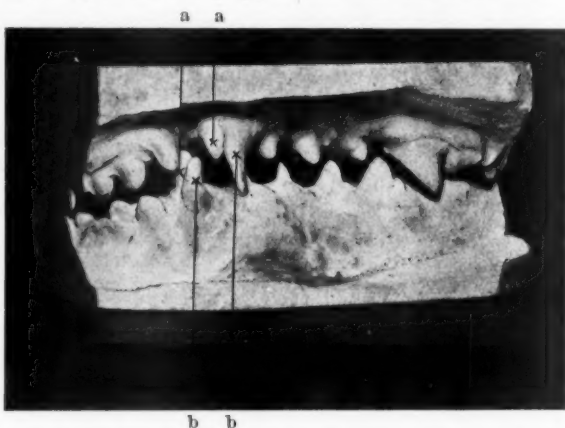


Fig. 11. A cast of the left half jaw of Per during the shedding of teeth. It is seen, that both in the upper as in the lower jaw the permanent canine tooth (a) is erupted in a mesio-lingual position to the temporary one (b), which still is persisting. Furthermore is noticed that the incisors of the upper jaw are in distinct lingual occlusion. The puppy is 6 months old.

oestrus which normally occurs in dogs at the age of 1 year had not appeared in Sonja when chloroformed 16 months old.

These two puppies were killed 16 months old. Serum Ca and P were normal. A chemical analysis of the middle third of the mesial metatarsal bone from the right hind leg demonstrates plainly that the bones were still not normally calcified, see table 20, p. 67. From this table it is further evident that there is a great difference in the figures for Per and Sonja. The figures of Per — except Mg — are below those of Sonja.

Table 20. Analyses of a Metatarsal Bone from Sonja and Per 16 Months Old.

	Pet. ash of dry w.	Pet. Ca of		Pet. P of		Pet. Mg. of	
		dry w.	ash	dry w.	ash	dry w.	ash
<i>Lisa.</i>							
Normal	64,6	26,2	40,7	11,1	17,4	0,28	0,48
<i>Sonja</i>	55,0	23,1	41,6	9,4	17,0	0,27	0,49
Pet. difference from normal	÷ 14,9	÷ 11,9	+ 1,9	÷ 15,3	÷ 5,0	÷ 3,5	+ 2,1
<i>Per</i>	48,7	19,9	40,8	8,2	16,8	0,28	0,57
Pet. difference from normal	÷ 24,6	÷ 24,0	+ 0,2	÷ 26,2	÷ 6,2	0,00	+ 18,7

F. inst. the pct. of ash: 48,7 and 55.0 respectively. The pct of Ca: 19,9 and 23,1 respect. and the pct. of P: 8,2 and 9,4 respect.

It is somewhat astonishing that these two dogs born and nursed by the same mother and afterwards given exactly the same food nevertheless show this difference in composition of the same bone. It is rather difficult to tell what the exact cause of this is. As an explanation we want to mention that Per grew more rapidly than Sonja. From clinical as well as from experimental studies of rickets we know that the most severe form of the disease develops where the increase in weight has been most rapid.

In order to throw some more light if possible, on this question we have performed some histological studies of the internal glands: The thyroid, the thymus and the pituitary glands. Gross histological changes, however, could not be demonstrated in these organs.

Ground specimens of the permanent teeth from Per, Sonja, and Bitten show marked hypoplastic conditions, see figs. 12, 13 and 14 on plates IV, V and VI. On the pictures we find thin and poorly calcified enamel and large and numerous inter-

globular spaces in the dentin. The teeth from the dog Per show the worst condition. Fig. 15, plate VII, is a ground specimen from a normal dog. We notice here the regularly calcified enamel and the regularly calcified dentin without any sign of interglobular spaces.

When the experimental mother animal, Lillemor, had finished the lactating period, the general condition of the animal was so poor that 250 cc. of milk had to be added to the usual ration every day. The condition of the bitch improved somewhat and after a normal resting period for dogs, the bitch was again mated with the same male dog as before. From this time the amount of milk given was reduced to 100 cc. and after 1 week the milk intake was stopped. This ration however was given just a few days as the dog's condition grew worse, 100 cc. of milk had again to be added to the diet.

We were not able to perform metabolism studies during gestation this time as the animal refused all food while in the cage. Thus no information as to the intake and output of the dog could be obtained. The blood analyses showed normal figures.

After 9 weeks of gestation the animal gave birth to three normally looking puppies which however had a considerably lower birth weight than the puppies of the first litter. While the youngs of the first litter weighed 370 ♀, 400 ♀, 390 ♂, and 440 ♂ gm, those of the second litter weighed 190 ♀, 270 ♀, and 310 ♂ gm.

One of the puppies of the second litter, *Fritz*, was chloroformed at once and examined in the same manner as Paal of the first litter. Tables 15 p. 52, 16 p. 54 and 17 p. 55 show the results. With the exception of the mandible most of the figures for this puppy are below those of Paal. Of the remaining 2 puppies, one died 3 days after birth, and the last died 5 days after birth. On section no gross pathological changes were observed.

An analysis of the milk from Lillemor 5 days after del-

ivery showed very low figures for Ca and P: 0,043 % and 0,040 % respectively. That is, the Ca and P values were reduced to about $\frac{1}{10}$ of the normal figures. The Mg content was not so much reduced: 0,0095 % against 0,011 % to 0,016 % (compare the figures in table no. 14, p. 51).

Thus we see that the condition of the mother, and still more the condition of the youngs, had been aggravated since the first delivery. The youngs of this litter were not able to live. Still we could not demonstrate any direct gross pathological changes in the body causing death. This condition may very well be compared with the condition of »congenital debility» in infants. Very often the autopsy report is quite negative in this condition too.

2. *Mineral Deficiency.*

The factors we have been working with in the reported experiments were mainly two: a salt deficiency (Ca and P) and a vitamin deficiency: (A and D) in order to place the experiments so near up to the conditions in practical life as possible. As a result of this deficiency marked changes occurred in the bones of the mother as well as in the bones and the teeth of the offspring: in the mother as an osteomalacia, in the offspring as a marked and early development of rickets.

In the first part of this report: metabolism studies on women, we observed that the negative Ca and P balance in some cases was improved by vitamin D addition, but in most cases remained negative or unchanged after such an addition. Evidently it was the deficiency in minerals which was the main lacking element in the diet of many of the women. According to this finding, we now wanted to see experimentally what effect such a deficiency in Ca and P alone might cause in the mother as well as in the offspring.

An experiment was performed parallel to the one described above on the same experimental diet (p. 45) only with 10 cc. of cod liver oil daily given to a bitch throughout the whole gestation and lactation period. Metabolism studies were as

Table 21. Metabolism Studies during Gestation of the Dog Stella.
(Ca and P deficiency).

Week of gestation	Minerals studied	Intake gm.	Output			Balance gm.	Pr. 100 cc. serum	
			Urine gm.	Feces gm.	Total gm.		Mgm. Ca	Mgm. P
1	Ca:	0,1574	0,0178	0,2117	0,2295	÷ 0,0721	10,4	3,6
	P:	0,2885	0,4007	0,1213	0,5220	÷ 0,2385		
	Mg:	0,1020	0,0823	0,0477	0,0800	+ 0,0220		
2	Ca:	0,1728	0,0380	0,0797	0,1177	+ 0,0551	10,4	3,3
	P:	0,3310	0,5600	0,1123	0,6723	÷ 0,3413		
	Mg:	0,1413	0,0447	0,1453	0,0900	+ 0,0513		
3	Ca:	0,1372	0,0480	0,2410	0,2890	÷ 0,1518	10,2	3,2
	P:	0,2933	0,4800	0,1803	0,6603	÷ 0,3670		
	Mg:	0,1503	0,0410	0,0777	0,1157	+ 0,0346		
4	Ca:	0,1182	0,0393	0,1533	0,1926	÷ 0,0744	10,2	3,1
	P:	0,1992	0,4500	0,1233	0,5733	÷ 0,3741		
	Mg:	0,1045	0,0517	0,0577	0,1094	÷ 0,0049		
5	Ca:	0,0629	0,0023	0,0970	0,0993	÷ 0,0366	9,5	3,4
	P:	0,1245	0,1500	0,0617	0,2117	÷ 0,0872		
	Mg:	0,0645	0,0080	0,0240	0,0320	+ 0,0325		
6	Ca:	0,1779	0,0157	0,1670	0,1827	÷ 0,0048		
	P:	0,3468	0,3433	0,1367	0,4800	÷ 0,1332		
	Mg:	0,1544	0,0357	0,0537	0,0944	+ 0,0600		
7	Ca:	0,1779	0,0197	0,1837	0,2034	÷ 0,0255	9,0	3,3
	P:	0,3468	0,5333	0,1127	0,6460	÷ 0,2992		
	Mg:	0,1544	0,0353	0,0280	0,0633	+ 0,0911		
8	Ca:	0,1779	0,0383	0,1805	0,2188	÷ 0,0409	9,5	3,2
	P:	0,3468	0,2633	0,1122	0,3755	÷ 0,0287		
	Mg:	0,1544	0,0373	0,0517	0,0890	+ 0,0654		
9	Ca:	0,1882	0,0145	0,0827	0,0972	+ 0,0910		
	P:	0,3785	0,3433	0,0850	0,4283	÷ 0,0498		
	Mg:	0,1827	0,0477	0,0363	0,0840	+ 0,0987		

Table 22. The Status of the Dog Stella at the End of Gestation.
(Ca and P deficiency.)

	Ca gm.	P gm.	Mg gm.
Total intake during gestation . . .	9,6486	18,3566	8,3283
Loss through urine and feces . . .	11,6042	31,7824	5,3901
Loss through the 6 fetus	13,9584	9,1602	0,5453
Total loss during gestation	25,5626	40,9426	5,9354
Balance at the end of gestation . .	÷ 15,9140	÷ 22,5860	+ 2,3929

before performed in three days periods during the whole 9 weeks of gestation. The results may be seen from table no. 21, p. 70. With exception of the second and the 9th gestation week when a positive Ca balance occurred the Ca and P balance was negative in every experiment. Table 22, p. 71 gives a summary of the metabolism experiments during the gestation. We find here a loss of about 16 gm. of Ca and about 23 gm. of P. That is even more than for the first experimental bitch, Lillemor, (Ca, P and vitamin-deficiency), with a loss of 15 gm. of Ca and 19 gm. of P. See p. 49.

After the normal gestation period the dog gave birth to 6 puppies.

We were not able to perform any metabolism studies during the lactation period of this dog as it was very difficult to separate the mother from the youngs.

The condition of the bitch was good throughout the whole gestation as well as the lactation period. The blood analyses performed every week showed but little lowering what the Ca is concerned. The figures for the Ca content of the milk was rather low at the 25th day after birth (0,217 gm.) but increased to the normal level at the 31st day after birth (0,331 gm.). The figures for P were all somewhat low compared with those of a normally fed dog, see table 14, p. 51.

After the end of the lactation period a corresponding metatarsal bone was resected and examined chemically as done for the first experimental dog. The result of the chemical analysis may be seen from table 13, p. 50. With the exception of Ca of ash all figures were below those of the control dog, (Lisa). The percentage difference from normal is though smaller than for the first experimental dog, (Lillemor II).

As mentioned before the bitch gave birth to 6 well developed and normally looking puppies with a birth weight of 295, 415, 326, 373, 374, 289 gm. They were all males. One was found dead. One was chloroformed for chemical analysis of the bones as well as of the whole body as was done in the preceding experiment. The remaining 4 puppies succed their mother, and 2 of them were after the end of the lactation period given the same diet as their mother.

We have seen that this low Ca and P content of the diet had influenced the composition of the mother's bone, though in a less degree than for the first experimental animal. The next question was to determine if this diet deficiency also influenced the youngs. They all looked quite normal and roentgenologically no anomaly of the bones could be detected.

A chemical analysis however of the femur of one of these newborn puppies, *Stegg*, see table 15, p. 52, showed a marked difference from normal, a difference which in some respects (when % Ca, P, Mg of ash is excepted), is even higher than for the newborn puppy of the first litter of Lillemor (the first experimental dog). The figures for the mandible indicate a change in the Ca, a small one, none in the P and Mg content, see table 16, p. 54. By examining the whole body of this puppy, *Stegg*, see table 17, p. 55, we found a distinct lowering for all determinations of Ca and P when compared with the normal puppy Lord.

Thus we see that a low Ca and P diet during gestation and lactation, even when plenty of all vitamins are given, is able to produce a chemical change in the composition of the bones of the mother animal, and, furthermore, a distinct lowering of Ca and P of the bones and the whole body of the

newborn puppy. We want to remind of the fact that this diet contained an amount of Ca and P pr. Kg. not lower than commonly found in the diet of the women examined above.

A proof is given that the composition of the bones of newborn animals may be influenced by the mother's diet being deficient in mineral substances alone.

The remaining 4 puppies nursed their mother, and after the end of the lactation period 2 were given the same diet as the mother. The 2 other puppies were used for other purpose. The 2 first mentioned puppies developed quite well during the lactation period of 5 weeks. The weight curve of these puppies was better than that of the puppies of the first experimental dog, see fig. 16, p. 74. 2 months old however they showed difficulty in walking. The hind legs were stiff and a couple of weeks later the puppies were not able to walk and were lying down most of the time. The legs showed some bowing though not much, and there was hardly any enlargement of the epiphyses.

Xrays taken regularly every week from the 65th day did never show ricketic lesions in the epiphyseal line, but during the 3 last weeks fractures of the femur could be detected. Ca and P analyses of the blood during the post-lactation period gave the following result:

Table 23.

Age in days		65	72	79	86	91	98	105	112
		Mgm. pr. 100 cc. serum							
Tell:	Ca:				8,6	8,0	8,4	9,1	8,5
	P:				5,6	7,8	6,9	7,6	7,0
Bobb:	Ca:	10,5	9,9	9,9	9,1	10,1	10,4	9,9	
	P:	8,5	8,2	8,5	6,7	7,6	6,8	7,2	

As is evident from this table, 23, the Ca content showed a faint lowering and the P content was also at a subnormal value.

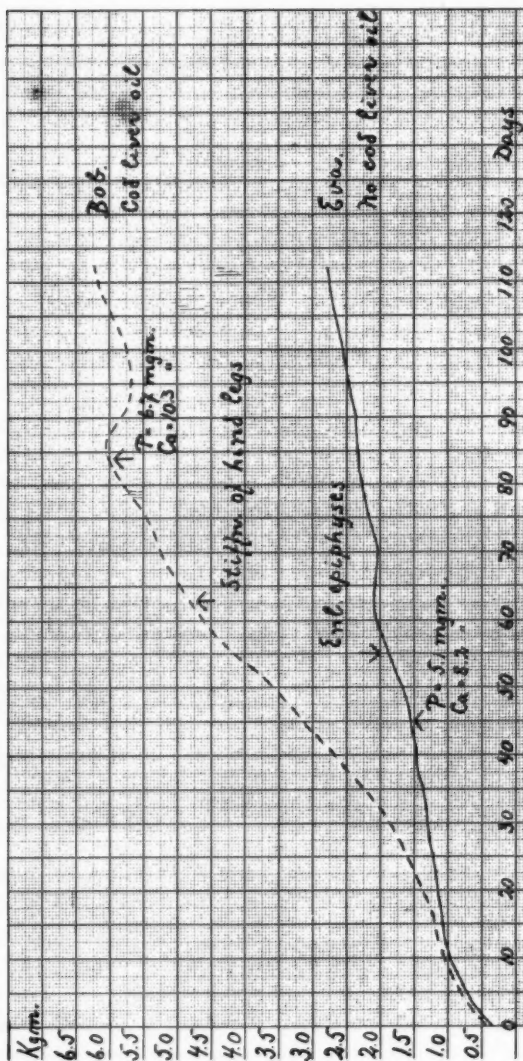


Fig. 16. Weightcurve of Bob: Ca and P deficiency, and Eva: Ca, P and vitamin A and D deficiency, during fetal and lactation period and later. Notice the marked difference in gain in weight and the different time for development of the pathological symptoms.

112 days old the puppies were killed. Post mortem X-ray examinations revealed multiple fractures of the hind legs, especially of the femur. The epiphyseal line was straight and there was no macroscopical sign of rickets, see fig. 17, plate VIII.

By chemical analysis of radius from these puppies a distinct difference from the normal was found what may be seen from table 18, p. 58. We find here that the figures for the puppy Bob are mostly below those of Tell¹ and for both these puppies we find the figures at about the level of those from the puppy Grete (Ca, P and vitamin deficiency from the beginning of the nursing period). Some of the figures are found to lie above, others below the last mentioned ones.

Thus no principle difference can be found between the chemical composition of the bones from the typical ricketic puppies and from these other puppies not showing distinct symptoms of clinical rickets. The difference is just a quantitative one. Another proof is given of the fact that chemical inferiority of the bones may be found in growing animals in spite of the X-rays revealing normal epiphyseal lines.

Special Description of the Histopathology of the Bones

given by dr. med. K. HÄUPL.²

Bock's method has been used as this method is well fitted to demonstrate the difference between the bony tissue calcified in vivo and not calcified in vivo. The bone specimens to be examined are hardened and fixed in a mixture of 5 % formalin: 1 part and Müller's fluid: 3 parts. After decalcification with 5 % Nitric acid which must not be carried on longer than to the point when it is just possible to cut the bone, they are imbedded in celloidin. With Hansen's hematoxylin the bone calcified in vivo becomes blue as the calcium during fixation combines with chromic acid and gives a blue color

¹ May be explained by the fact that Bob gained more rapidly in weight than Tell.

² We hereby extend our best thanks to dr. HÄUPL for his valuable help in preparing the material and describing the results.

with this dye. The bony tissue uncalcified in vivo becomes red with the following eosin treatment.

In order to get a good result some calcium salts must be present after the decalcification process. Otherwise all bony tissue will get a red color.

The microscopical examination of a metatarsal bone from the first experimental bitch (Lillemor) gave the following results: Fig. 19, plate X demonstrates the metatarsal bone resected before the gestation period. On the surface several osteoblasts are noticed and below this a narrow layer of uncalcified bone. The osteoid zone measures here 5–6 μ .

Fig. 20 is a microphotograph of a corresponding metatars resected after the end of the lactation period. We notice here the very thickened uncalcified zone measuring 50–60 μ in diameter. We often find Howships lacunae and large osteoclasts together with marked changes in the bone marrow. The usual fatty tissue is mostly changed to oedematous fibrous tissue. Small hemorrhages are here noticed many places. These changes in the bone marrow is evidently of secondary nature: a result of the increased mechanical pressure on this tissue through the deficiently calcified bone trabeculae. This picture is histologically to consider as an *osteomalacia*.

The histological sections of the metatarsal bones, resected before and after the reproductive cycle, from the second experimental mother animal, *Stella*, do not differ very much. The sections from the last resected bone show somewhat enlarged osteoid zones on some places. The bone marrow doesn't appear to be affected at all.

The examinations of the bones from the newborn puppies: Lord, Paal, Fritz and Stegg of which Lord represents the control puppy, gave practically identical results. (As will be remembered from the chemical analyses, see table 15, 16, 17 the bones of Paal, Fritz and Stegg showed a definite deviation from normal in its composition of ash, Ca and P). The osteoid zone measured in average 10–20 μ , maximum 40 μ . The bone marrow was of a myeloid character and rich in blood cells. Around the muscle-insertions, however, fibrous marrow could

be detected. A faint histological difference between the control puppy and the experimental puppies may perhaps be said to exist as the latter show a tendency to hyperemia as well in the femur as in the mandible and especially in the dental pulps.

Examinations of the bones from 112 days old puppies Lisken, Siss, Grete, Eva, Bob and Tell gave the following result:

In the control animal, Lisken, the uncalcified zone is about 10 μ broad, see fig. 21, plate XII while the uncalcified dentin is 20—30 μ . The bone marrow consists mostly of fatty tissue. In some places we may see rests of myeloid tissue, and small amounts of fibrous tissue. This may be seen from the picture taken from the subchondral bonetrabeculae of the radius. The thickness of the cartilage-proliferative zone was in the average 90 μ .

In the experimental puppies we find a perfectly different picture: In the bones from *Siss* (Ca, P and vitamin A and D deficiency from the end of the nursing period), the newly formed uncalcified zone measured about 40 μ and the cartilage-proliferative zone 2—6 mm. The fatty tissue in the bone marrow was mostly replaced by fibrous tissue what may be seen from fig. 22 which is taken from the ulna. Even more marked changes were noticed in the bones and teeth from the puppy *Grete* (Ca, P and vitamin deficiency from the beginning of the nursing period). The uncalcified zone measured here 80—90 μ and the dentinoid zone averaged 100 μ . On fig. 23, plate XIV is plainly seen in the light part of the section the thickened, uncalcified zone of dentin and to the left a narrow stripe of calcified dentin. Smaller and larger calcospherites are seen scattered throughout the broad dentinoid zone. The cartilage-proliferative zone measured 4—6 mm. It has also to be mentioned that there was considerable fibrous tissue throughout the bone marrow, furthermore, hemorrhages besides hyperemic dilated vessels. As far as the next puppy, *Eva*, (Ca, P and vitamin deficiency from the beginning of the fetal life) is concerned the partly completely uncalcified bone trabeculae

measured about 140 μ . Such bone trabeculae are seen in fig. 26, which demonstrates a periosteal bone apposition at a muscle insertion. From this picture it is evident that the completely uncalcified, the gray trabeculae, are arranged in the direction of the muscle fibres. In the bone marrow is seen only fibrous tissue and plenty of hyperemic dilated vessels. The cartilage proliferative zone measured 6 mm.

In the last two puppies, Bob and Tell, (just Ca and P deficiency from the beginning of the fetal life) the findings are somewhat different from those of the three last described puppies: The epiphyseal line is possibly slightly thickened. The uncalcified zones in the bone as well as in the dentin from the puppy Tell are clearly detectable, but not at all so predominating as in the puppies: Siss, Grete and Eva (mineral and vitamin deficiency). In the puppy Bob somewhat enlarged osteoid zones may be found. See figs. 26, 27, plates XVII, XVIII.

The bone trabeculae from both these puppies are furthermore thin and relatively few compared with the control puppies. This picture corresponds mainly to a bone hypoplasia (osteoporosis) though combined with an increased formation of osteoid tissue. See fig. 18, plate IX.

As to the explanation of the histological findings from the experimental animals of the first group the most essential feature in the picture is the thickened uncalcified zone, which may be 10 times the normal. This points in the direction of conditions being present in the organism which prevents the deposition of calcium salts in this newly formed uncalcified bone.

The nature of the cause cannot be explained on the basis of just histological sections. So much can, however, be stated that the cause is not to be found in the bone itself — that is: The first formed bone matrix is not unable to receive and fix the minerals — but the cause must be sought for outside the bony system. (The skeleton of adults is also in a state of constantly rebuilding).

In full harmony with this we find that the thickness of

the uncalcified zone in the three experimental puppies: Siss, Grete and Eva is least in the first and greatest in the last mentioned one. This is furthermore in complete harmony with the chemical examinations (see table 18). As will be remembered the deficiency started for Eva during the fetal life, where as for Siss it started at the end of the lactation period.

The fact that the experimental newborn puppies did not show any enlarged osteoid zone in spite of a subnormal calcification being detected by chemical analyses, may be explained as follows: A quantitative difference in the calcification is more easily detected by a chemical analysis than by a histological examination. The latter method only demonstrates the fully uncalcified bone and not the just partly uncalcified one, and the pathological process in the fetus might not have been so extensive as to lead to such a pronounced defective calcification.

As far as the findings in the puppies: Siss, Grete and Eva are concerned, namely: the formation of fibrous tissue, periosteal bone formation (see fig. 24, plate XV) and the thickened proliferating zone of the cartilage, it is to be mentioned that these must not be considered as primary but as secondary changes. They are functional disturbances caused by the fact that the deficiently calcified bone is not resistant enough to stand the functional-mechanical irritaments from outside. Some bonetrabeculae are particularly exposed and here a periosteal boneformation is seen. In this way we may explain the periosteal boneformation.

The thickened proliferating zone of the cartilage is probably explained by a poor calcification not only of the bone but also of the layer of cartilage above the proliferating zone what will result in an increased mechanical pressure on the proliferating layer.

The formation of fibrous tissue in the bone marrow with hemorrhages and hyperemic conditions of the vessels are above explained by the increased mechanical pressure on the marrow-spaces through the deficiently calcified bonetrabeculae.

C. Comment.

These experimental studies have shown that a diet somewhat low in Ca, P and vitamin A and D during gestation lead to a marked loss of Ca and P from the body, furthermore to a low Ca and P content of the blood, to development of tetany during lactation and to a marked chemical and microscopical change of the bones corresponding to the picture of osteomalacia. The puppies of this bitch showed a lowering of the Ca and P content of the bones at birth and later an early and severe form of rickets with marked signs of poor calcification of the teeth.¹

It is furthermore shown that the time for the development of the ricketic process may under otherwise equal postnatal conditions be determined by the time when the deficient feeding starts in the mother animal.

When the deficiency of the diet during gestation just was a mineral one (Ca and P) similar chemical changes in the bones have been produced in the mother animal but in less severe degree than was the case in the first one. Chemical changes were also present in the newborn puppies at birth. These puppies did not however develop marked clinical symptoms of rickets but multiple fractures of the legs with just the same chemical changes: A lowering of the Ca, P and Mg content of the bones, as in the ricketic puppies and a microscopical picture corresponding to a hypoplasia or an osteoporosis with slight ricketic changes (thickened osteoid zones).

It cannot be denied that the difference between these two litters is a great one. In the first litter we find the symptoms considered as typical for rickets: distinct swelling of the joints, beading of the ribs, bowed legs, lowering of the inorganic elements of the blood, irregular epiphyseal line

¹ According to BLOCH and M. MELLANBY vitamin A has no direct influence on the calcification of teeth. As the diet, however, for the women and experimental animals is low in both fatsoluble vitamins, A as well as D is mentioned.

and post mortem findings of enlarged osteoid zones and lowering of the inorganic elements of the bones. In the second group we find as the main symptoms: Stiffness and infractions of the legs, slight swelling of the joints, slight beading of the ribs (particularly in Tell) a faint lowering of the inorganic elements in the blood and post mortem findings of bone hypoplasia with slight formation of osteoid tissue and a lowering of the inorganic elements of the bones. The difference in the clinical picture may be quite marked, the result for the animal is the same: invalidity.

Thus these studies indicate that a diet deficiency during pregnancy whether this is a mineral (Ca and P) and vitamin (A and D) deficiency, or just a mineral deficiency has a definite influence on the offspring. As far as the vitamins are concerned we are now used to talk about a store, and for vitamin D the liver is supposed to be the main store house. As is mentioned below, it is a question if not the subcutaneous tissue is a store house for D as well as for A. When the diet is low in this vitamin D during pregnancy, the store at birth is low, and when the post natal feeding also is deficient or lacking this vitamin, it is evident that the symptoms of a deficiency, in this case, rickets, will appear earlier the less the store is at birth.

As is the case with vitamin D so it evidently is with all the other vitamins.

We are not so well used to talk about a store when the minerals are concerned, but it seems to us that both of these calcifying factors may be looked upon from the same point of view. Keeping the recent investigations of Aub, Bauer and Albright in mind the store house for Ca is the bone trabeculae, and in cases where the diet during pregnancy has been low in minerals Ca, and P, the trabeculae are few and the store of Ca is low. If the postnatal feeding also is low in minerals, we will have a development of an osteoporosis or an osteoporosis combined with a mild rickets as for the second litter.

If the post natal feeding is sufficient in minerals but lacking in vitamin D which probably is nearer up to the practical

life, what is then the result? We are not able on the basis of these experiments to tell whether or not such a congenital osteoporosis is a predisposing factor to an early development of rickets, the old question thouroughly discussed by Wieland (5). On the basis of clinical investigations he came to the result that an osteoporosis (craniotabes) does not dispose to development of rickets whereas Abels and Hughes (64, 65) are of different opinion. See below. Experiments on dogs in order to study this particular question are now going on and will be published later.

V. General Discussion and Practical Application.

A. Rickets.

The first part of this work: Investigations on women, has shown that women, living on a food which may be characterized as a quite common one in this country, often gave a negative Ca and P balance during the 2—3—4 last months of pregnancy.

In some cases this negative salt balance evidently was due to a low intake of fatsoluble vitamins as an addition of vitamin D improved the negative balance. In most of the cases, however, a low Ca and P intake was the essential cause. As far as we can deduct from our investigations on women, the daily Ca intake ought not fall below 1,6 gm. and the daily P. intake not below 1,8 to 2,0 gm. If the diet then contains plenty of fatsoluble as well as watersoluble vitamins, the Ca: P relation is optimal and the diet is basic, the Ca and P balance may be positive under otherwise normal conditions. Does the mineral intake fall below this amount, a vitamin addition alone is usually not able to make the balance positive. This high minimum amount of the salts is evidently necessary to cover the daily need during the two last months of pregnancy.

The occurrence of this negative balance falls together with the period when the essential part of the bones and teeth of the fetus is under calcification.

The second part of these investigations were performed on dogs in order to follow the eventual effects of the above stated diet deficiencies on the mother and youngs. The deficient diet had naturally to be used throughout the whole gestation and lactation period of the mother animal.

In the first experiment where both Ca, P and vitamin A and D were deficient, the mother suffered a considerable

loss of Ca and P during gestation and lactation, also demonstrated chemically on the bones. Tetany developed in the mother, and the youngs showed chemical changes of the bones at birth. Rickets developed in the youngs at a very early stage and earlier than in puppies born by a mother normally fed during gestation, but then given the deficient feeding, showing the importance of the diet deficiency during gestation.

When the deficient feeding was started in the youngs at the weaning, the ricketic symptoms appeared still later than when the deficiency started at birth. Under otherwise equal conditions the time for development of ricketic symptoms may thus be directly determined by the duration of the deficient diet, not only during the post lactation period, but also during the lactation period as well as during the fetal life. We further have to notice that the youngs of the second litter were much underweight and all died a few days after birth. Similar results are also demonstrated by one of us on rats (48).

The second experimental animal where the diet was deficient just in Ca and P suffered also a considerable loss of Ca and P as a result of the gestation and the lactation period. On the newborn youngs definite chemical changes were demonstrated. These youngs however did not develop distinct rickets but a marked osteoporosis, or hypoplasia with slight ricketic changes resulting in multiple fractures of the hind legs.

The question now is if these findings in the women and dogs may have any applications to the conditions in practical life. What we are particularly interested in is to know whether or not these experiments may contribute somewhat to the explanation of the predisposing causes of the two common diseases affecting particularly the bones and teeth of the child, namely *rickets* and *dental caries*.

As far as rickets is concerned, it is rather difficult in practical life to draw any definite conclusions as to the influence of the fetal period on the development of rickets in infants.

We have mentioned earlier that by our clinical methods used on the newborn infant, with a few exceptions (see p. 7), no

information has hitherto been given as to the changes which may have taken place as a result of the conditions in fetal life.

During the last year we have performed some roentgenological studies of the epiphyses of radius and ulna and the metacarpal bones of some of the infants from the examined mothers. The infants have been from 5—17 days old. On these infants we have been able to see a distinct difference in the calcification at the end of the epiphyses especially of the metacarpal bones. In cases where the nutrition of the mother has been poor during pregnancy, particularly as far as the minerals and the vitamins are concerned, the epiphyses are fringy and poorly calcified. That is usually the case in infants from mothers who have not stayed in the home after regulation of the diet for any length of time before delivery.

A far better calcification of the epiphyses was noticed in infants from mothers who have stayed in the home several months before delivery. These studies have been performed during the fall of 1930 after the diet of the home was regulated. As is reported in the first part of this paper this regulated diet gave mostly a positive Ca and P balance even during the last 2 months of pregnancy. In near relation to the development of these epiphyses the calcification of the skull is going on. This is only just a preliminary report of these studies which have just been started. They will be published later in extenso when completed.

In the work by Coons and Blunt (26) similar changes were observed in the epiphyseal ends of the diaphyses of 8 days old infants from mothers with poor retention of Ca and P during pregnancy.

The main cause of the negative results of earlier authors in this respect has evidently been the mode of examination. They have been looking for typical ricketic changes. Furthermore no attention has been paid to the prenatal feeding in the individual cases. The changes found by Coons and Blunt and by us are not marked but though clear enough and are closely parallel to the feeding of the mother.

However interesting these findings in infants are, we must

be fully aware that the roentgenological and even histological examinations may be entirely negative, and never the less changes may have occurred in the bones which may influence the disposition to rickets if the postnatal feeding is not ideal.

This is evident from our experimental studies on dogs. Even in cases where the disposition to rickets was very marked as in some of our experimental puppies, the Xrays of the bones at birth were negative. The same was mostly true as far as the histological studies were concerned. Just by chemical analyses of the bones of the newborn puppies we were able to detect the pathological changes resulting from the diet deficiency during the fetal period. These chemical changes (a low ash, Ca and P) together with a low store of the vitamin D in the body must have predisposed the puppy to the development of the very early and severe rickets. As we remember the ricketic symptoms appeared much earlier in these puppies than in those born by a mother normally fed, (see p. 57).

We consider it rather natural that the same may be the case in human beings. Even if none of the usual ricketic symptoms are detected in newborn infants, nevertheless, the disposition may be present and eventually detected by chemical analyses of the bones as in our experimental animals.

Other evidences of a disturbance going on in the organism predisposing to the development of rickets may also be present. We want here to mention that a negative Ca and P balance was found in three to six weeks old athreptic infants examined by one of us (55). In such infants a distinct lowering of serum P was found. A figure as low as 2,2 mgm. P pr. 100 cc. serum was once observed. There were no other clinical signs of rickets at that time in these athreptic infants.

The interesting finding of JUNDELL and MAGNUSSON (*Acta Paediatrica* IX, Fasc. 1—2) of higher P content in umbilical cord blood from infants born of mothers given cod liver oil during pregnancy compared with infants from mothers not given cod liver oil is of importance to remember in this connection.

In close relationship to the above mentioned findings we want to remind of the rather scanty occurrence of macroscop-

pical hypoplasia and much more frequent occurrence of microscopical hypoplasia of the deciduous teeth (80 % of all deciduous teeth are hypoplastic according to M. Mellanby).

We know that the formation of these hypoplasia must have taken place in fetal life. This condition therefore is the most evident clinical proof that disturbances in the calcification process is of frequent occurrence in fetal life. They must evidently be considered under the same point of view as the roentgenological changes noted by us in newborn infants just that the latter disappear very quickly but the former are persisting.

Also GYÖRGY (56) in his recently published monograph pays much attention to this finding in teeth and thinks that the question of congenital rickets on the basis of this must be reconsidered. He writes: »Werden diese Befunde und ihre Deutung einer Nachprüfung in der Zukunft standhalten, so würde auch das Problem der angeborenen Rachitis, das bis vor kurzem noch als entschieden galt, von neuem an Aktualität gewinnen».

The relatively frequent cases of rickets in breastfed infants depend certainly in many cases on the low vitamin D content of the mother's milk. Besides this factor a disposition to the disease from fetal life plays without doubt a great rôle.

Twins and premature infants are highly disposed to rickets. Often so disposed that an ideal postnatal feeding is not able to prevent a mild occurrence of this disease in such infants. According to HESS and CHAMBERLAIN (57) rickets was found in premature infants fed ideally from birth and even exposed to ultraviolet radiation from the 14th day of life. According to CAPPER (58) rickets was observed in nearly all of the premature infants examined.

In both cases, twins and premature infants, we evidently are dealing with a deficient calcification. In the first case because two fetus are to be built up from a store which in some cases may be insufficient for even one, and in the second case, because the fetus has not had the opportunity to be completed on account of an interrupted fetal period.

When HESS, WEINSTOCK and SHERMAN (59) has found a normal amount of vitamin D in the liver of premature infants, it does not prove that the premature infant's organism contains a sufficient amount of this vitamin. According to POULSSON (60) vitamin A may be contained in the subcutaneous tissue. The same may hold true for vitamin D. Premature infants are usually of a slender type with a minimum amount of subcutaneous fat. If then this supposition is correct, the liver may contain the same amount of vitamin D for premature as for full term infants and yet a great difference may exist in the store of D in the whole body.

That the liver is an unreliable storehouse for vitamin D, Hess, Weinstock and Sherman give an example of by reporting »a splendid child» weighing 11 kgm., who »had received three teaspoonful of cod liver oil daily for almost two mos. previous to the time of death». »The liver in this case was found lacking in antirachitic factor.» In such a case f. inst. the subcutaneous tissue might be the real storehouse for the antirachitic vitamin.

Even in fullterm infants a distinct disposition to rickets may be noticed. This is particularly true for cases where the nutrition of the mother during pregnancy has been poor.

A severe rickets was thus observed in a 15 months old infant who had been given breastmilk from birth and mixed vegetable- fruit- cereal- and milk diet with cod liver oil daily from 6 months of age. Otherwise he had been under the best hygienic conditions. The mother of this infant, however, had been ill throughout the whole pregnancy and on account of constant vomiting had retained very little food. The cod liver oil treatment of the infant from the appearance of the first ricketic symptoms had evidently been of little effect.

Whether or not it is the low mineral store or it is the low store of vitamin D which is of greatest significance in the early development of rickets in the infants we are not able to tell just on the basis of these experiments. We know that a Ca and P deficiency alone with plenty of vitamin D during pregnancy and lactation and during the growth after the end

of the lactation period gives a picture which does not show the typical changes which we are used to call rickets, but produce a marked osteoporosis leading to multiple fractures of the bones. The typical epiphyseal changes observed by clinical, roentgenological and histological examinations are certainly associated with a vitamin D deficiency. A pure salt-deficiency occur perhaps very seldom in practical life. A Ca, P and vitamin D deficiency are usually combined both in the pre- and postnatal period of the infant. As we may deduct from our experiments on women however it is the Ca and P deficiency which is the most prevalent in the prenatal period. In the postnatal period the vitamindeficiency is perhaps the most essential. For artificially fed infants at least we know with certainty that this deficiency plays the greatest part.

In breastfed infants however, it is not impossible that a deficient Ca intake may play a part besides a vitamin D deficiency. From table 9 p. 39 we see that the Ca content of women's milk may vary within wide limits from 18 to 31 mgm. percent on the usual diet of the home. Furthermore we see that the Ca content of the women's milk may increase to 42 mgm. percent on a diet rich in Ca. Such wide variations may influence the calcification process of the infant.

As HOFMEISTER (61) has pointed out on the basis of investigations by ARON (62), a new born infant contains an average of 0,9 % Ca of body weight. If this relation is to be kept up (in the organism of adults the figure is 1,45 %) it is not small quantities of breastmilk which is required to meet the demand. On the basis of a birth weight of 3 000 gm. a newborn infant contains 27 gm. Ca, and if the infant gains 30 gm. a day (for some infants this is somewhat high) about 0,9 % of this must be Ca (=0,27 gm.) which corresponds to about 1000 gm. of human milk. Just very few infants take such a high amount, at least during the first weeks of life. »The infant therefore is under the danger of too low Ca intake during the first months of life» as Hofmeister expresses it. If we consider this calculation to be right, we find that the Ca intake through breastmilk from a mother on a poor

diet sometimes may be too low just as well as the other factor, the vitamin D content, also may be low.

In practical life we thus may find a Ca and P deficiency prevalent in prenatal life and a vitamin D deficiency prevalent in postnatal life, besides a possible Ca deficiency in some breastfed infants. A pure salt deficiency has according to our experiments mainly resulted in an osteoporosis, a vitamin D deficiency in addition has given typical epiphyseal changes with excessive formation of osteoid tissue. These conditions can not be differentiated chemically, they have both given a lowering of ash, Ca and P. The fragility of the bones may as we have seen, be extreme in a clear cut osteoporosis. The characteristic changes at the growth centers of the long bones, the swelling of the epiphyses, were lacking.

These investigations point in the direction of showing that the group of symptoms called rickets may not be a disease *per sé*. It may partly be an osteoporosis, mostly perhaps caused by a mineral deficiency during pregnancy, and partly an osteopathy with typical ricketic changes (osteoid tissue) mostly caused by a vitamin D deficiency during the pre- as well as the postnatal period of the infant's life.

The craniotabes so much discussed in the pediatric literature may possibly be explained on the basis of such an osteoporosis in the infant, caused by a mineral deficiency in the diet of the mother. The congenital craniotabes thoroughly investigated and discussed by WIELAND (63) was found to occur in 20% of all newborn infants. He found in 1910 by histological examination that this congenital craniotabes was caused partly by »ungenügender Bildung normalen Knochens» and had nothing to do with rickets at all. It did not even predispose the infant to rickets. A later development of craniotabes is neither considered pathognomonic for rickets: JUNDELL (64).

ABELS and KARPLUS (65) hold a different point of view. The last authors have found that the infants born with a soft skull are much more disposed to rickets than the infants born with a hard skull. The figures are according to these authors 84%

and 12 % respectively. The congenital craniotabes is therefore considered by them as a »Prärachitische Osteoporose».

As to the causative factors HUGHES (66) as well as ABELS (67) believe that a mechanical pressure in the uterine life is of importance for the development of the localized soft areas of the skull. But then Hughes writes: »Though the great majority of individuals are subject to closely similar mechanical conditions, only a minority, say one fifth, develops cranioathrophy to the clinically recognizable degree. In this minority therefore, decalcification¹ must be promoted by some morbid agency.» He then discusses the possibility of lues or rickets being the cause. Then he continues: »With this particular problem, however, observation can do little and we await the results of the experimentalist, especially on such subjects as the effects on the fetus of illbalanced diets involving deprivation of vitamin A (1921) and the causes of osteomalacia.»

We have reported the result of such an experiment earlier in this monograph.

At present we are investigating the bony system of newborn infants at the same time as mineral metabolism studies have been performed during pregnancy on the mothers, see p. 85. The result of this study will appear in a later publication.

ABELS (68) has furthermore noticed that deformities of the skull of newborn are only observed in infants with poor calcification of the skull. He is of the opinion that these common deformities are the result of the mechanical pressure in uterus on infants with a poorly calcified skull. It is furthermore reported that such poor calcification is particularly noticed in infants from the cities and especially in infants born at winter time and early spring time.

During the last year there have appeared several publications dealing with different form of rickets, particularly one form with low calcium content of the blood. Recently BLOCH and FABER (69) described a mild form of rickets with hypocalcemia and normal serum phosphorus, corresponding fairly

¹ The authors of this monograph do not agree in this expression.

well to the description of earlier cases by McCOLLUM, SHIPLEY, PARK, HESS and coworkers.

The most essential clinical symptoms in the cases of Bloch and Faber was a craniotabes and a slow closure of the fontanel. These cases were often suffering from tetany. Bloch and Faber mention among other factors the possibility of a deficient supply of the boneforming salts during the fetal life as an explanation to the condition.

When we now know that such a deficiency is of quite frequent occurrence the supposition of Bloch and Faber is rather strongly supported.

In practical life we have to remember that a vitamin D deficiency is often present and is apt to occur if not a special regulation of the diet has been performed. Among the common food articles we know that milk and vegetables, except for the summer time, contain just small amounts of this vitamin. Egg yolk is the only one which contains a larger amount of D. As eggs however, are rather expensive and largely considered as luxury in this country, particularly during winter time, the common diet will usually be low in this vitamin.

Many infants are evidently born with a rather low store of Ca and P as well as of the vitamin D. It depends then to a great extent on the postnatal feeding whether or not this store of the different calcifying factors will be repaired to meet the daily demand of the infant when the necessary retention for a normal growth is taken into account.

Is the store of vitamin D very low at birth, the postnatal feeding, even ideal, may not be able to compensate for this low congenital store of the calcifying factors and rickets develop never the less, especially when the growth is proceeding rapidly as for instance in the above reported 15 mos. old boy. Such is evidently the case in many premature infants, also in the cases described by Hess and Chamberlain where rickets developed in spite of irradiation by ultraviolet light from the 14th day of life.

B. Dental Caries.

While the ricketic bone changes may be repaired comparatively quickly in many cases when the postnatal feeding is good, and the deformities will disappear, most changes taken place in the teeth remain there for life. These are the macro- and microscopical hypoplasia in the enamel and dentin which have mostly the same causes as the ricketic bone changes. Such deficient calcification occurs in the pre- as well as in the postnatal period.

This marked difference in the reaction of bones and teeth is without doubt due to the quantitative difference in the metabolism rate of the two different tissues.

We know that these macro- and microscopical hypoplasia formed during the calcification period of the teeth render them less resistant to caries. This is a common clinical experience, see among others BILLING (70), (we sometimes find the opposite to be true, and many are of the opinion that ricketic teeth are not more prone to decay than other teeth) and also statistically proved especially by May Mellanby, see table 2 p. 11. We also want to remind once more of the writings of O. Walkhoff from 1895 (15): »Der Weg zur Einschränkung der Zahnkaries kan nur mit Erfolg beschritten werden, wenn die Praedisposition der Zähne nach Möglichkeit fortgeschafft wird. Die Praedisposition hat aber ihren hauptsächlichsten Grund in den Entwicklungsfehlern der harten Zahngewebe».

An examination of the deciduous teeth as well as of the six year molars from children of the previously examined mothers, would be of great significance in throwing light on the influence of the prenatal period for the condition of these teeth.

Considering the pathological picture, caries dentium, postnatal influences as feeding, general and especially local hygienic conditions play an important part and may even be the dominating factors, but as far as the hypoplasia are concerned, they will remain undisturbed by post eruptive influences.

Among factors which may have a disturbing influence on the formation of teeth during the intra as well as the extra uterine life, many could be mentioned besides the two dealt with in this paper: a deficient mineral and a deficient vitamin intake. In order to be able to judge the importance of these factors, we have examined some children with their mothers at the Children's Department of the Dental School of Norway.

The mothers were thoroughly examined as far as diet, disease and general condition were concerned during pregnancy and lactation. Thorough information was obtained as to the feeding, disease and development of the child from birth to the day of examination. The child was then given a physical examination, a tuberculin test performed on all children, hemoglobin determination (Sahli) if the children were pale. All children were weighed and measured, and the result transferred to SCHIÖTZ (71) height—weight charts used in the public schools of the city of Oslo.

As to the diet of the mothers during pregnancy we were particularly interested in the amount of milk, what kind of bread and whether or not vegetables and fruit were taken daily. The mothers were always able to tell whether or not milk, fruit and vegetables were a part of the every day diet, just as well as they remembered what kind of bread was usually eaten. As far as the amount of these different food articles was concerned, they were not able to state the exact amount taken, but by thorough examinations they were usually able to tell the average amount, at least of milk. As far as the calcium intake is concerned the milk is of the most dominating influence, as 70—80 % of the total Ca intake is usually derived from this food stuff, ABRAMSON (72). By such an examination we found that the mothers as a whole may be divided into two parts: one group taking milk with appetite and without any difficulty, and another group who do not like it, and «get an indigestion» from it, and therefore use just a minimum of it in the every day diet. If the mothers belonging to the last group under usual conditions made some use of it, a

large number stopped using it when the pregnancy started, mostly on account of constipation. None of the women had taken lactic acid milk in order to overcome this difficulty. Besides the milk used for breakfast and supper, the milk used in preparing the food was also counted. The first group, counting the mothers who took $\frac{3}{4}$ —1 liter of milk daily, consisted of just 10 %. The rest of the women either did not drink milk at all (about 25 %) or used less than $\frac{1}{2}$ liter daily. The milk products, such as cheese and »prim» which are good sources of Ca were not used daily.

The bread mostly eaten was made of finely milled rye and wheat, (the commonly used bread in Norway now-a days). Just a few mothers used whole wheat bread. There is of course a difference in the Ca content of these two kind of bread. According to our own analyses, the first contains as an average 0,023 % Ca and the whole wheat bread 0,034 % Ca. When the bread is prepared with milk, the difference in the Ca content between the two sorts of flours will be of no practical importance. White bread prepared with milk, showed a Ca content of 0,08 % as an average value.

The vegetable intake was quite small, just the women with pregnancy period during the summer and fall used some vegetables daily. The fruit intake was also by most of the women wholly dependant on the typical seasons.

From informations given by the mothers to 90 children hitherto thoroughly examined we may conclude with certainty that about 90 % had a calcium intake not exceeding 0,7—0,8 gm. daily during the last half of the pregnant period. (Besides these mothers to 90 children, 50 other mothers are examined from the same point of view, and with the same result).

From the metabolism studies on pregnant women described in the first part of this paper we know that a Ca intake of 0,7—0,8 gm. does not cover the daily need and will give a highly negative Ca balance during the 2—3 last months of pregnancy. The P intake by the mothers was calculated to a somewhat higher figure due to the large consume of bread and meat. The figure however usually did not exceed 1 gm.

P pr. day for most of the women, and thus will give a negative P balance according to the above recorded metabolism studies.

The vitamin intake by most of the women must also be characterized as insufficient as far as C and D (and perhaps also B) are concerned

During the lactation period the average amount of milk taken was higher than during pregnancy. The Ca and P intake were not far below the optimum amount during this time. (A lower amount of Ca and P is needed to cover the output through the milk, than to build up the fetus during the last two months. Nevertheless, we have to remember that the mother's organism needs a rather high amount of these minerals during this time in order to repair the possible existed negative Ca and P balance during pregnancy.) The vitamin intake during lactation has mostly been lower than during pregnancy as many mothers were afraid of eating fresh fruit and vegetables thinking it might hurt the infant.

The children of these mothers were examined as to caries, and macroscopical hypoplasia. The age of the children ranged from 3—14 years. As the frequency of caries varies according to age, the children had to be divided into age groups. Our material as yet is insufficient to form any definite conclusion and we just want to mention the direction in which these investigations go: Children from mothers living on a minimum amount of milk (below $\frac{1}{2}$ l.) during pregnancy showed double as high incidence of caries in the teeth formed during this time, as did the children whose mothers had lived on a high milk-vegetable-fruit diet.

70 % of the children showing a macroscopical hypoplasia of the enamel of the permanent teeth have received artificial feeding (Nestlé food or oatmeal-milk mixtures) in stead of breastmilk during the first $\frac{1}{2}$ to 1 year of life. The other 30 % showing such defects have received mothers milk 2—3—4 months and 1 child was given this feeding all first year. Nevertheless this child had had a severe rickets according to the

descriptions given by the mother. The examination also proved this to be the case.

The metabolism disorder given rise to these hypoplasia (formed postnatally) is hardly caused by a deficient mineral intake, but with all probability by a deficient intake of vitamins, particularly vitamin D. The artificial food has been prepared in such a way (long time boiling) that we may suppose that the vitamins even if they formerly were present in a sufficient amount have been destroyed to a considerable degree. It is a great question if the cow's milk, particularly during the winter time, really contains enough of the various vitamins for the infant even without going through any heating process.

We will now shortly record some typical cases from these examinations.

E. S. a 7 years old girl. Macroscopical hypoplasia of the enamel of all deciduous teeth, the 4 six year molars and the two permanent incisors in the lower jaw (the only permanent incisors erupted), see fig. 28, plate XVIII.

As may be seen from the picture cavities are present in practically all fissures and pathological pits in the six year molars and the deciduous teeth. The mother gave the following information: She never drank milk, not even during pregnancy and used very little milk in preparing the food. She did not like milk. Some fruit and vegetables were used, but not much. Vomited very often and felt weak.

The child was a full term infant. No breastmilk. Was given »Nestlé» in milk until 1 year of age, then the infant was given a mixed diet, but with very little fresh food. No cod liver oil. From 2 years of age the child has not had any milk to drink. The usual diet has consisted of:

Breakfast: White bread with coffee.

Lunch: Sandwiches with coffee.

Dinner: Meat and fish with vegetables and soup.

Supper: Sandwiches and coffee.

8 months old the child got scarlet fever. Quite often infections of eyes and ears.

The main cause of the poor conditions of the teeth is without doubt: insufficient amount of mineral salts during fetal life, in-

sufficient intake of vitamins during the first year and insufficient intake of mineral salts besides from the age of two years. The scarlet fever has probably augmented the other pathological factors.

A. S. a 7 years old boy: 13 cavities in the deciduous teeth and 10 in the six year molars, see fig. 29, the left picture. The mother gave the following information: She used some milk, about two glasses daily during pregnancy. Very little fruit and vegetables.

The child was a 2 months premature. (Birthweight 1750 gm.) Breastmilk 6 months, then breastmilk + »Nestlé» until 1 year of age. Then mixed diet with practically no fruit and vegetables. No cod liver oil. Took quite much milk during the preschool age.

He had frequent colds during the first year. A mild bronchitis 14 months old.

Comment: The deciduous teeth were not very bad for this age, but the six year molars were very poor, pulp exposure in both of the lower 6 year molars. The mineral and vitamin intake during the calcification period was low.

The conditions during the formation of the occlusal surface of the six year molars were extremely poor. As the infant was 2 months premature, the calcification of these teeth had supposedly just started, and according to what is emphasized earlier in this work, such infants very seldom escape rickets even when they are breastfed.

H. S. a 6 years old girl, sister of the preceding one. 35 cavities in the deciduous teeth (no permanent teeth were erupted). From fig. 29 the right picture, we may see that the crowns of all the 4 incisors in the upper jaw were completely destructed, just the roots were left. She had not a single sound tooth. The mother gave the following information:

She did not take any milk during pregnancy as she had an eruption which she supposed was due to milk in the diet. She ate very little fruit and vegetables and during the three first months of pregnancy she nursed her first boy. She vomited very often during the first 4 months of pregnancy and felt weak throughout the whole period.

The child was a fullterm infant. Breastmilk besides »Nestlé» was given the first year. No other food until 1 year of age. From this time she took much milk but very little of fruit and vegetables. She contracted a mild form of measles $\frac{1}{2}$ year old.

Comment: Very poor teeth. Rather low amount of mineral salts and vitamins during fetal life. As the mother nursed her first boy the first months of her second pregnancy and for a long time had lived on an insufficient diet, there had been no time

for repair. The infant's food during the first year was also insufficient.

A. S. 4 years old, brother of the two foregoing children. 4 small cavities in the fissures of the deciduous teeth. The mother gave the following information: She took at least 1 liter milk daily. Fruit and vegetables were as before used very seldom. The mother felt well throughout the whole pregnancy. The child was a fullterm infant. Breastfed until 6 months. Cream of wheat until 11 months when he was given mixed food. After 1 year of age he took as his brother and sister $\frac{3}{4}$ —1 liter milk daily. No diseases.

Comment: Good teeth. The dietetic conditions during the formation of the teeth were good as far as the mineral intake is concerned. The vitamin intake probably low.

These three children and the condition of their teeth are quite noteworthy. The Caries frequency varies very much — for the deciduous teeth 4—13—35 cavities. The difference in age, 4—7—6 years, can not, as the conditions are here, play such a dominating rôle that a comparison is not allowed. The local hygienic conditions have been uniform for all three children. None of them has had severe infections or other diseases, influencing the metabolism or accompanied by poor local hygiene of the mouth. A's bronchitis and H's measles during infancy were both mild infections. The dietetic conditions after birth have been practically alike for all three children. None of them have shown difficulty in taking food and none of them have shown any particularly like or dislike to certain food articles. After the formation period of the teeth in question it has not been any perceptible difference neither local or general between these three children which may be thought of as a cause of the great variation in the frequency of caries. When, however, the prenatal period is considered, the calcification period of these very teeth, a noticeable difference is present. The child showing the best teeth has also had the best developmental conditions during fetal life as far as the nutrition and the general hygiene of the mother is concerned, and the opposite: the child with the poorest teeth has also had the poorest developmental conditions during fetal life.

H. N. a 9 years old boy. No information as to the frequency of caries of the deciduous teeth can be given, as he had shed most of them. The six year molars and the permanent incisor teeth show marked macroscopical hypoplasia of the enamel with caries in all fissures and in practically all pathological pits of the enamel, see fig. 30.

The mother gave the following information: She used boiled milk, but very little fruit and vegetables during pregnancy. The child was a full term infant. No breastmilk. Oatmeal and milk boiled 20 min. was given during the whole first year. No addition of fresh food until 2—3 years of age. The boy has taken much milk later. He was healthy throughout the pre-school age. 7 years old he contracted measles. The boy had a typical ricketic skull. His two brothers, one older and one younger, showed exactly the same dental conditions and they had been fed in the same way.

Comment: The occlusal, respectively incisal third of the permanent teeth were poorly calcified and showed marked caries. These parts of the teeth were formed at a time when the diet was highly insufficient in vitamins. Besides the deficiency in vitamins we also have to consider the oatmeal in the diet. Especially through the investigation by M. MELLANBY both on dogs and on children (16, 82) and by others f. inst. G. TOVERUD (48) we know the deleterious effect on the teeth by a high oatmeal diet when the vitamin D is low. Thus we may in this case also take into account a possible toxic factor.

G. O. a 10 years old girl. The deciduous teeth had been shed. All six year molars, the permanent incisors and canines show marked macroscopical hypoplasia of the enamel with deep caries in all fissures and in nearly all indentations of the enamel, see fig. 31.

The mother gave the following information: She took much milk throughout pregnancy but felt weak and vomited all 9 months of the pregnant period. She retained very little food. The child was 2 weeks premature. Breastmilk 4—5 months, then cream of wheat. 6 months of age she got mixed food. Started to walk rather early, but stopped and did not start again until 1 1/2 years old. Pertussis accompanied by a severe pneumonia 2 years old. She stayed in bed for many weeks and became rather emaciated. She did not recover before 9 months had elapsed.

Comment: The mother of this child felt sick with constant vomiting throughout pregnancy. A hypocalcification or at least a disposition to such was evidently present in the infant at birth.

The diet during the first year was fairly good, but nevertheless, it had not been sufficient after such a fetal period to prevent rickets. The girl did not walk until 18 months of age.

It is evident from the picture that the most marked defects are found on that part of the crowns which according to the calcification table reproduced on page 12, should be under calcification when the child was between 2 and 3 years old.

In this case it is evidently not a primary nutritional disturbance which has caused this poor calcification of the teeth, but a severe infection with a secondary influence on the intermediary metabolism. (We can naturally not evaluate the possibility of a low food intake during such conditions). We know well from the literature that acute as well as chronic infections may have a disturbing influence on the mineral metabolism. As far as the teeth are concerned pertussis seems to be a frequent cause of a deficient calcification.

An old supposition is that a tuberculous infection has a predisposing effect on the development of caries. In the following case such an infection has evidently played some rôle.

T. O. a 6 1/2 years old boy. 30 cavities in the deciduous teeth and marked hypoplasia of the enamel together with deep caries in all six year molars (penetration to the pulp in two of them), see fig. 32 to the left. (Other permanent teeth were not erupted).

The mother gave the following information: She used some milk, but not so much as 1/2 liter daily during pregnancy. Used plenty of natural butter. Very little fruit and vegetables. The mother was suffering from tuberculosis since she was 14 years. A severe hemoptysis 4 months pregnant. Felt fairly well the rest of the time. The child was a full term infant. Eruption of the teeth at 4—5 months old. Started to walk when he was 1 year old. Not breast milk, but »Nestlé» for 7 months, then oatmeal with milk and cream of wheat. Some fruit during the first half year. In the preschool age he took much milk and plenty of fruit and vegetables. Used bread of finely milled rye. The boy had pertussis and measles at 1 year of age in a very mild form. At the examination he showed a strongly positive Pirquet reaction. No abnormalities by physical examination of the lungs were noticed.

Comment: Both deciduous and permanent teeth were poor. On account of the tuberculous infection of the mother, the calcification of the deciduous teeth as well as of the occlusal part of the six year molars had gone on during very difficult conditions.

The diet during this time was also deficient. The same

may also be said to be true during the first part of the post-natal developmental period of the six year molars. The mild infection at 1 year of age has hardly played any significant rôle. As the boy did not present any symptoms of tuberculosis (besides the positive tuberculin test) it is hardly necessary to think of any such infection.

The other 6th year molar, to the right, on fig. 32 also shows a deficient development of the enamel as the foregoing. This tooth is extracted from a 5 $\frac{3}{4}$ years old boy (E. B.).

All of the temporary molars were so badly decayed that full amalgam crowns had to be put on, and in each of the other deciduous teeth two or three cavities were present. The six year molars had already erupted and showed a marked hypoplastic condition with extensive caries in all. In the two lower ones the pulp was infected. Figs. 33 and 34 demonstrate very clearly the microscopical hypoplasia in the enamel as well as in the dentin.

The mother gave the following information: Milk, fresh fruit and vegetables were almost entirely omitted during pregnancy. She often vomited. The child was one month premature. No breast-milk, only »Nestlé» the whole first year. From this age a mixed diet was given, but no cod liver oil and very little fresh fruit.

Comment: Very poor teeth. The nutrition of the mother had been very deficient in minerals and vitamins. The postnatal feeding had also been highly deficient, especially in vitamins.

As is evident from these few examples from our material, a high cariesfrequency with or without hypoplasia of the enamel has been found in children where informations as to dietetic conditions during the developmental period are given which we know affect badly the calcification of the teeth. These deficiencies in the diet have been an insufficient intake of mineral salts or insufficient intake of vitamins. Cases are also reported showing with all probability the causal connection between infectious diseases during the developmental period, and the poor calcification of the enamel. (Whether or not the vitamin deficiency and the infectious diseases influence the tooth formation directly or indirectly through the ductless glands will not be discussed here).

As mentioned before, we must of course not disregard the dietetic and the local hygienic conditions after the erup-

tion of the teeth as such factors are of great influence in determining the status of the teeth. As to the first point, concerning vitamin D, M. MELLANBY and C. PATTISON (73) *int. al.* have made some very interesting observations: They have found a smaller amount of new caries points in children whom for a certain time had been given a vitamin D rich diet, compared with children given a vitamin poor diet. The caries frequency at the beginning of the dieting period was practically alike for the two groups just as well as the conditions otherwise were the same in both groups and as by most children. Besides a lower incidence of new caries, it was found in the first group a retardation of the carious process in the dentin with hardening of the previous soft dentin. The secondary dentin in the vitamin D rich group was furthermore better formed than in the other group. We have also observed several similar cases and we will report one case which illustrates this point very well:

In a two years old illegitimate girl all deciduous teeth had erupted with the exception of the four second molars and the two lateral incisors in the upper jaw. (Later one of the latter showed to be absent.) The crowns of both first molars and of both the middle incisors in the upper jaw were completely destructed with exposed pulps. Extensive caries and decalcification areas were also present in all other teeth.

Comment: As the mother had tried to hide her pregnancy, she had lived in a poor condition and her diet had been very deficient.

Immediately after birth the infant was put in a private home where the artificial feeding was very insufficient. The hygienic conditions otherwise were also poor. The infant had shown an early rickets with anemia which had lasted throughout infancy. When 2 years old the child was adopted, and given a well regulated diet. The teeth were properly treated. From that time the child has lived under the best hygienic conditions. 2 years have now elapsed from the first treatment of the teeth, and not a single cavity nor the slightest chaulky spot has appeared.

The enamel which at the first treatment was rough and dull and could be scratched by a probe, has now a hard, smooth and lustrous surface.

Although the subject is not included in the title of this monograph, a few words ought to be written about the dental condition during *pregnancy*. The old saying: »A tooth for a child«, has been discussed for many years both by the dental and the medical profession, some believes in it, and others not. No definite conclusive statistics have been published as far as we know which would settle the question. It is however a common observation that the teeth are more liable to decay during pregnancy than during other periods of about the same age. Some of the few statistics at hand also confirm this. Many authors (see literature: KARLSTRÖM (74), TOVERUD, G. (75) suggest the cause of this high incidence to be the great demand of Ca for the fetus. This supposition must be said to be strongly confirmed by the results of the present investigations. We find that women are apt to live in a negative Ca balance during the last $\frac{1}{3}$ of the pregnancy unless they take a liberal amount of food rich in minerals. In such cases the women have to give off minerals. By this negative balance the blood, saliva and the tissue fluids will be altered in composition. The circulating fluids in the teeth (BÖDECKER, 76), as well as the saliva will contain a smaller amount of basic elements and thus have a smaller buffer value. We have earlier in this monograph referred to such findings, but want once more to stress the examinations of BECAS (38) showing that the average Ca content of the saliva during the last part of pregnancy is not more than 50 % of the normal value. The Na and K content is also lowered. The value of Ph goes in the same direction: 7,153 as the normal figure and 7,05 during pregnancy.

Furthermore an acidosis, a decrease in basic elements and a relativ increase in acid factors (OARD and PETERS 77) is commonly met with during this period.

In a discussion of the subject: Dental Caries, TÜRKHEIM (78) is not of the opinion that pregnancy disposes to decay, and he writes: »Wahrscheinlich ist dies nicht der Fall, und zwar aus folgenden Gründen: es wird angeführt, das der zum Aufbau des Foetus notwendige Kalk dem mütterlichen Or-

ganismus entzogen wird, also auch den Zähnen der Mutter. Es müsste also vorausgesetzt werden, dass Kalkmangel die Kariesdisposition schaffe, und dass ferner kariöse Zähne kalkärmer sind als resistente. Für beide Prämissen fehlt bisher irgendein experimenteller oder sonstiger Beweis.»

As we have pointed out above (p. 104) a negative balance during pregnancy may act in another way than that quoted by Türkheim and nevertheless give rise to a high caries incidence.

The few records at hand of the result of a preventive treatment of pregnant women by calcium salts also point in the same direction. Among such records that of KIRSCH (79) is rather interesting: »Eine Reihe von Schwangeren während der Gravidität wurden untersucht, und in sechs Monaten einen Verlust durch Karies von 3,82 Zähnen pro Patient festgestellt; Kontrolluntersuchungen bei anderen Graviden, die Kalkpräparate bekamen, zeigten nur einen Verlust von 1,75 Zähnen pro Patient.»

The above reported investigations also throw some light on the very early occurrence of deformities of the jaws in infancy. KONTOROWICZ and KORKHAUS (80) have demonstrated compression of the upper jaw on casts from infants as early as 37 days after birth. They state that the cause of this anomaly is the normal sucking action on an *abnormally* soft jaw bone. This deficient bone structure can hardly be caused by a postnatal metabolism disturbance. An inferiority of the bone or at least a disposition to subnormal calcification has certainly been present at birth.

The majority of orthodontists consider rickets as an important factor in the etiology of the largest group of dento-facial deformities — the jaw compressions.

Not only rickets, however, but any condition causing an abnormally soft bony structure may naturally be a causative factor, ANDRESEN (81). Earlier in this monograph we have briefly discussed the condition craniotabes — osteoporosis — and pointed out possible etiological factors. The predisposing

factors for some of the dentofacial deformities may as for rickets, osteoporosis and partly for dental decay, be sought back in the prenatal period of the individual's life.

The poor development of the jaws and the irregulare shedding of the deciduous teeth are furthermore demonstrated in the puppies, se fig. 11, p. 66 and still better by M. MELLANBY, f. inst. (82).

The importance of correct feeding during fetal life as well as during the early infancy for the development and the structure of the jaw bones is also highly stressed by the well known pediatrician McKIM MARRIOTT (83).

Summarizing: Every preventive measure against rickets or any hypoplasia of the bones and against dental decay *is also an orthodontic prophylactic measure.*

As mentioned before in this monograph many authors have thoroughly discussed which factor is the chief causative one during the calcification period of the teeth to produce a predisposition to caries. ROSE (19) who has performed some of the most extensive researches on this problem, writes in 1908: »Wer seinen Kindern die Vorteile erdsalzreicher Ernährung sichern will, muss schon vor ihrer Geburt bei sich selbst mit der Zufuhr von Erdsalzen beginnen». This statement, very interesting to the last day, was however made before our knowledge of the accessory food factors. It has therefore now to be reconsidered.

WALKHOFF in his interesting monograph (18) pays nearly exclusively attention to the C vitamin and writes: »Für die möglichste Beseitigung der Praedisposition der Zahnkaries und ihrer eventuellen Folgen ist eine allzeit genügende Zufuhr von Vitaminen in intra und extra uterinen Leben des Menschen der ausschlaggebende Faktor. Letzterer bildet das Fundament für die Entwicklung und die Existenz eines guten Gebisses.»

MAY MELLANBY, the investigator who has done the most valuable work on the influence of vitamin D for the deve-

lopment of teeth, is also of the opinion that the vitamin intake is the punctum saliens in this respect. Opposite to Walkhoff, however she refers to vitamin D instead of vitamin C.

The fact that she does not stress the great value of the mineral intake, is the more surprising as the milk intake in England she says to be as low as 150 cc. pr. day and individual. Furthermore, Mrs. Mellanby in her regulated diets includes a good quantity of milk, f. inst. in one publication: (84) the daily diet of the group of children showing the best teeth contained 1023 cc. of milk whereas the diet of the worst group contained 511 cc. of »milk» and 140 cc. of »separated milk».

In the rather interesting series of publications by JONES, LARSEN and PRITCHARD (85) from the dental conditions in Hawaii the authors »suggest that these children (with the high percentage of odontoclasia) may be born with a mineral deficiency due to faulty maternal diet». By this faulty diet they almost exclusively think of an acid giving one. As far as we understand they do not pay much attention to the intake of minerals and vitamins, this notwithstanding the fact that they always find better teeth by the groups of people where the diet contains plenty of milk, fruit and leafy vegetables. Furthermore their general findings of much better teeth in the oldest children of a family compared with the younger ones very well may be explained on the basis of a mineral drainage of the mother. By the low intake of minerals and vitamins the store of the mother will become more and more depleted and less available for the fetus. A similar low store and intake of minerals by the young children of 1 and 2 years may also explain the extensive acute picture of odontoclasia at this time. The suddenly increased activity of the child with increased ratio of the mineral metabolism will naturally during such a low mineral intake cause a pronounced change in the fluids of the organism, f. inst. the saliva. An analysis of the blood and saliva in these children might possibly have thrown more light on this point.

The great caries frequency in children, suffering from tetany the first year of life (described by HJÄRNE (86)) may partly be explained on the basis of a low Ca and vitamin D store.

A broad view on the conception of the predisposing as well as of the direct causative factors to disturbances of the hard tissues of the organism is held f. inst. by ADRION (87), JEANNERET (88) and especially by the well known investigators in nutrition as SHERMAN (44), McCOLLUM (89), HOWE (17) and v. WENDT (90). They recommend a liberal amount of minerals and vitamins, a preponderance of lacto-vegetable diets which also will give the best conditions for an optimal acid-base balance.

VI. Summary.

In order to study the predisposing factors to rickets and dental caries 69 saltmetabolism experiments have been performed on 30 women living in a home for expecting mothers. The total intake and output of calcium, phosphorus and magnesium were determined for periods of 4 days during the last 2—3 months of pregnancy, in one woman from the third month of pregnancy. 17 women were given a diet used in the home for years, and which has to be considered as a quite ordinary Norwegian diet (p. 20).

A negative Ca balance was found in 21 and a negative P balance in 12 of 27 experiments in pregnancy. This negative balance could be made positive or less negative by increasing the calcium to 1.6—2 gm. and for phosphorus 1.8—2 gm. daily. Table 5 p. 22. This was done partly by increasing the quantity of milk in the diet, in one case by giving calcium as a special calcium lactate preparation (Kalzan). In a few experiments an addition of cod liver oil to the usual diet without increasing the Ca intake turned the balance over in a positive direction. In the majority of experiments cod liver oil or a vitamin D preparation (Vigantol) did not affect the negative balance at all when the Ca and P intake was low. Of the 12 metabolism experiments performed during lactation on 6 women, 4 gave a negative Ca balance and 6 a negative phosphorus balance. Table 6, p. 30.

The calcium content of breast milk from 14 lactating women on the same diet was found below normal, and could be increased by increasing the calcium intake in the diet. Table 9, p. 39. The P content, however, decreased in the majority of cases.

Metabolism experiments performed on 7—8 months pregnant women on a diet regulated as to contain above 1,6 gm. Ca and P, a liberal amount of vitamin D as cod liver oil with fruit and vegetables giving an alkaline ash have all given a positive balance. Table 8, p. 36.

When eggs were used as the source of vitamin D instead of cod liver oil by 6 women, a positive balance was also found. Table 8, p. 36.

In order to study in details what effect an unregulated diet used by the first women, that is, one low in Ca, P and vitamin D, might have on the mother and youngs, some experiments on dogs were started.

A bitch was given a diet low in Ca, P and vitamins A and D before and during gestation. By metabolism experiments on Ca, P and Mg performed in 3 days periods every week throughout the whole gestation, it was found that the bitch suffered a very great loss of Ca (about 10% of its original Ca content). During the lactation period 8 days after delivery, the mother animal developed tetany with a serum Ca of 5,15 mgm. and a serum P of 2,92 mgm. pr. 100 cc. Chemical analyses of a metatarsal bone resected before and after gestation and lactation showed that a great loss of Ca and P had taken place in the bone resected after the end of lactation. Table 13, p. 50.

X-ray pictures taken of the newborn youngs of this experimental bitch revealed no changes from normal. Microscopical examination of these bones gave just insignificant changes. By chemical analyses however a distinct lowering was found of the calcium and phosphorus of the femur as well as of the whole body. Tables 15, 16, 17, p. 52, 54, 55. Thus we see that only by chemical analyses it was possible to demonstrate the changes taken place.

The youngs which after 6 weeks of lactation were given the same diet as the mother, showed very early signs of rickets with marked deformities of the extremities. The rickets in these puppies was more pronounced and appeared earlier than in puppies born and nursed by a mother given the ex-

perimental diet from the day of delivery. These last puppies again showed a more marked rickets than puppies born and nursed by a mother on a normal ratio but given the experimental diet after weaning. Fig. 3, p. 56.

Chemical analyses of the bones from these three different litters of puppies performed at the same age (112 days) showed a calcium and phosphorus and magnesium content lower than normal, a lowering which corresponded to the difference in development of ricketic symptoms. Table 18, p. 58.

Microscopical sections of the same puppies showed typical ricketic changes corresponding in degree to the chemical picture. Figs. 21, 22, 23, 24, plates XII, XIII, XIV, XV.

X-ray pictures of the jaws and teeth of the puppies revealed a similar difference in tooth calcification and development. Figs. 5, 6, 7, plates II, III. Ground specimens of teeth show the same steps in calcification of enamel as well as of dentin. Figs. 12, 13, 14, 15, plates IV, V, VI, VII.

Another bitch was given the same diet as the first one just with cod liver oil added to the experimental ration which thus was deficient only in the minerals Ca and P. All steps in the experiment were repeated.

The blood Ca and P showed a small lowering during gestation, no tetany developed. A similar, just smaller loss of Ca and P was found to have taken place in a metatarsal bone from this bitch as in the first one after the end of the lactation period. Table 13, p. 50.

X-ray pictures of the newborn puppies revealed no changes from normal. Microscopical sections of the bones showed as for the puppies of the first bitch just insignificant changes. The Ca and P content of the femur as well as of the whole body showed a similar lowering as in the first experimental litter. Tables 15, 16, 17, p. 52, 54, 55.

The youngs after weaning given the same diet as the mother did not show distinct ricketic symptoms, but stiffness and soreness of the hind legs, by X rays showing to be caused by multiple fractures of the long bones. Fig. 17, plate VIII.

Chemical analyses of the bones from these 112 days old puppies showed a similar but smaller lowering of the Ca, P and Mg content. Table 18, p. 58.

Microscopical sections of the same puppies showed mainly a picture of a bone hypoplasia (osteoporosis) with slight formation of osteoid tissue particularly for one of the puppies. See figs. 18, 27, plates IX, XVIII.

The practical application of these metabolism experiments is then discussed as far as rickets and dental caries is concerned. The great difference in disposition to these two diseases in cases where the postnatal care have been alike, has been referred to an insufficient nutrition of the mother during pregnancy, which is illustrated by examples from practical life.

VII. Conclusions.

1. A negative Ca and P balance in women is often demonstrated during the last part of pregnancy and also, though less frequent, during lactation. The cause of this negative balance is chiefly a too low content of minerals in the every day diet.

A vitamin D deficiency besides other factors may also play a rôle.

2. A mineral and vitamin deficient diet during pregnancy and lactation makes the offspring predisposed to rickets and dental caries.

3. The prevention of these two diseases with all their sequels ought to be started in the fetal life.

The preventive measure includes the regulation of the diet of the pregnant and nursing women so as to contain $\frac{3}{4}$ —1 liter of milk, eggs, fresh fruit and plenty of different vegetables daily. During the dark season extra vitamin D addition in form of cod liver oil or irradiated ergosterol should be given.

Such a diet characterized chiefly as a lacto-vegetable diet with addition of vitamin D will contain a sufficient amount of minerals, vitamins and basic elements — the best conditions for a normal calcification to take place.

We hereby extend our best thanks to the chief of the Physiological Department of the University, professor, dr. S. Torup for the opportunity given to perform these studies at the Department and for the interest he has taken in the work.

The assistance of the staff of the Department is gratefully acknowledged.

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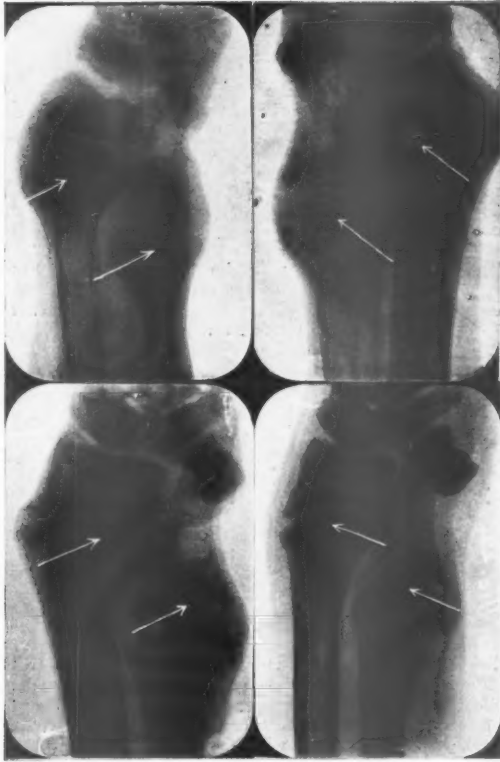


Fig. 4. Roentgenograms of radius and ulna from the 4 different puppies, the weight-curve of which is reproduced on fig. 3, p 56. The pictures were taken when the puppies were 112 days old. Upper, left: Eva, upper, right: Grete, lower, left: Siss and lower, right: Lisken (control).

II

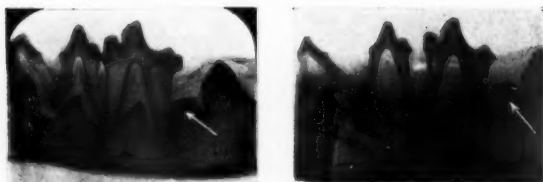


Fig. 5 a. Roentgenograms of the mandible bone from Eva, to the left, and Grete, to the right. The thickness of the calcified enamel-dentin cap on the tubercle indicated by the arrow (permanent tooth) is for Eva 1,5 mm and for Grete 2,0 mm.

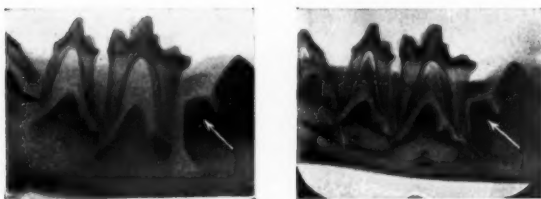


Fig. 5 b. Roentgenograms of the mandible bone from Siss, to the left, and Lisken, to the right. The thickness of the calcified enamel-dentin cap on tubercle indicated by the arrow (permanent tooth) is for Siss 2,3 mm and for Lisken 2,5 mm. Notice at the same time the thinner rootwalls of the deciduous teeth of Eva compared with those of Siss and Lisken. — Furthermore it may also be noticed the more crowding of the teeth in the jaw of Eva.

Diet deficiency see p. 57.
Compare also figs. 6 and 7.

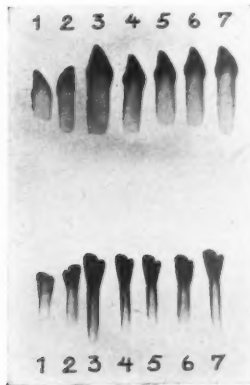


Fig. 6. Roentgenogram of the permanent mandibular I_2 from the experimental puppies: Eva No. 1, Grete No. 2, Siss No. 3 and Lissen No. 4. (Nos. 5, 6 and 7 do not belong to this study). The upper pictures demonstrate the lateral view and the lower ones the frontal view. It may plainly be seen from these pictures that the tooth from Eva (Ca, P and vitamin A and D deficiency from the beginning of the fetal period) is least calcified. The tooth from Grete is better calcified (Ca, P and vitamin A and D deficiency from birth) and still better is the tooth from Siss (Ca, P and vitamin A and D deficiency from the end of the lactation period). It is hardly any difference to be noticed between the latter tooth and the tooth from Lissen (normally fed).

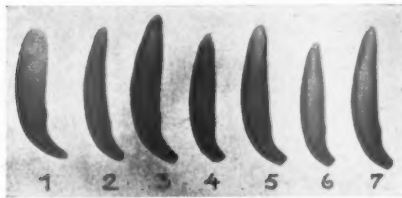


Fig. 7. Roentgenogram of the temporary canine tooth from the same experimental puppies as in fig. 6. The same steps in calcification may be noticed here as in fig. 6.

IV

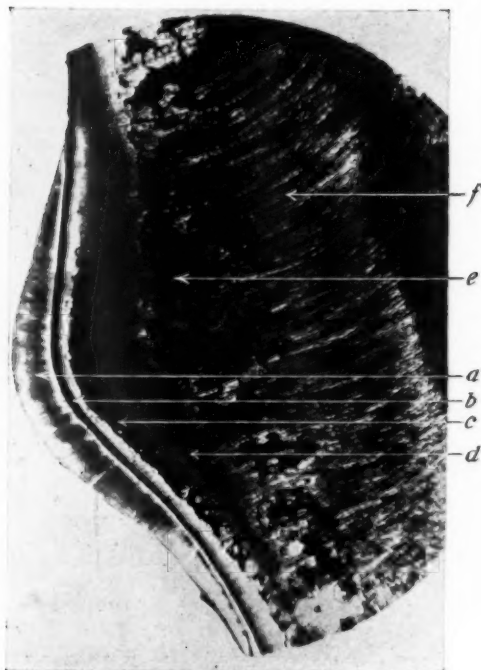


Fig. 12. A microphotograph of a ground specimen of a permanent front-tooth from Per: Ca, P and vitamin deficiency from start of fetal life. 35 times enlargement. The picture demonstrates from left: The enamel, poorly calcified (a), a stripe of fairly well calcified dentin (b), then a row of large interglobular spaces (c), a layer of fairly well calcified dentin (d), then again large interglobular spaces ($\frac{1}{3}$ of the dentin-thickness) (e) and finally a fairly well calcified dentin (f). Compare with fig. 15. See change in diet p. 62.



Fig. 13. A microphotograph of a ground specimen of a permanent front-tooth from Sonja, the same deficiency as for Per. The picture demonstrates from left: A poorly calcified enamel, a fairly well calcified dentin, a broad zone of large interglobular spaces, and finally a well calcified dentin.

See 67.



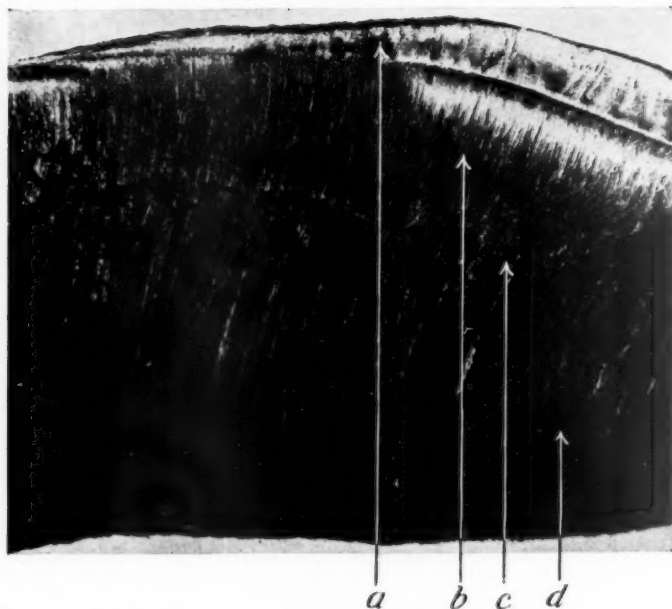


Fig. 14. A microphotograph of a ground specimen of a permanent front-tooth from Bitten: Ca, P and vitamin deficiency from end of lactation. 50 times enlargement. The picture demonstrates from above: The enamel, which is poorly calcified (a), a broad zone of normal dentin (b), then large interglobular spaces (c) and finally a normally calcified dentin (d).

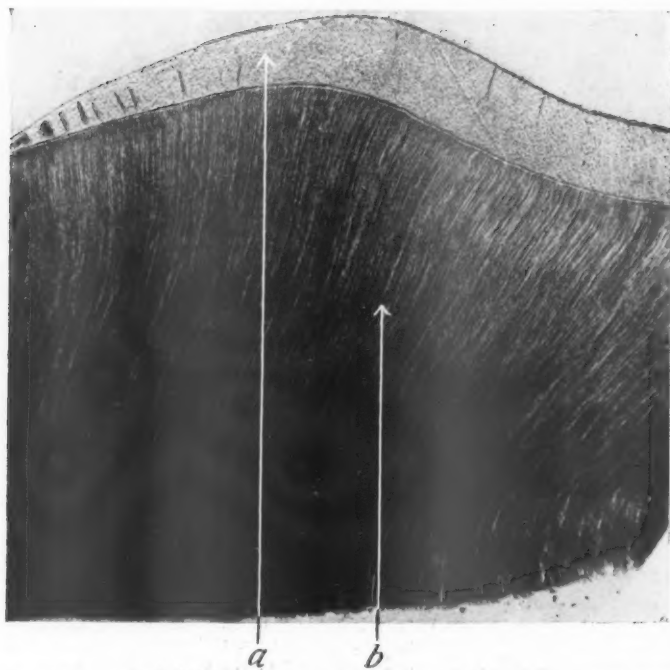


Fig. 15. A microphotograph of a ground specimen of a permanent front-tooth from a normally fed puppy. The picture demonstrates from above: The enamel, which is well calcified (a), the dentin, which every where shows a normal calcification without any sign of interglobular spaces (b).

VIII



Fig. 17. Roentgenograms of the hind legs of Bob (Ca and P deficiency). We notice the multiple fractures of both femur, tibia and fibula. The epiphyseal line is straight. No swelling of the epiphyses are seen.

See page 73.

Compare also fig. 18, pl. IX.

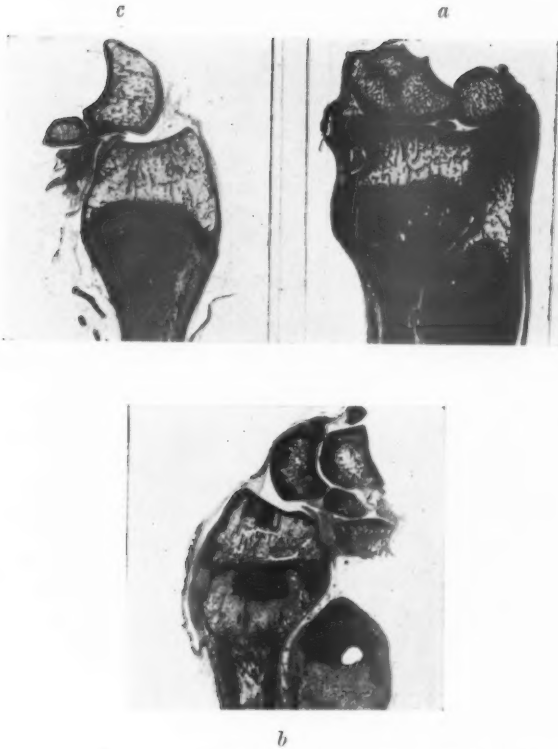


Fig. 18. The epiphysis of radius from: Lisken (a), normal diet during fetal life, lactation and later (Control puppy). — Eva (b), Ca, P and vitamin A and D deficiency during fetal life, lactation and later. — Bob (c), Ca and P deficiency during fetal life, lactation and later. Notice the wide proliferating zone of cartilage in Eva, and the scarce and thin trabeculae in Bob compared with those of the control puppy Lisken.

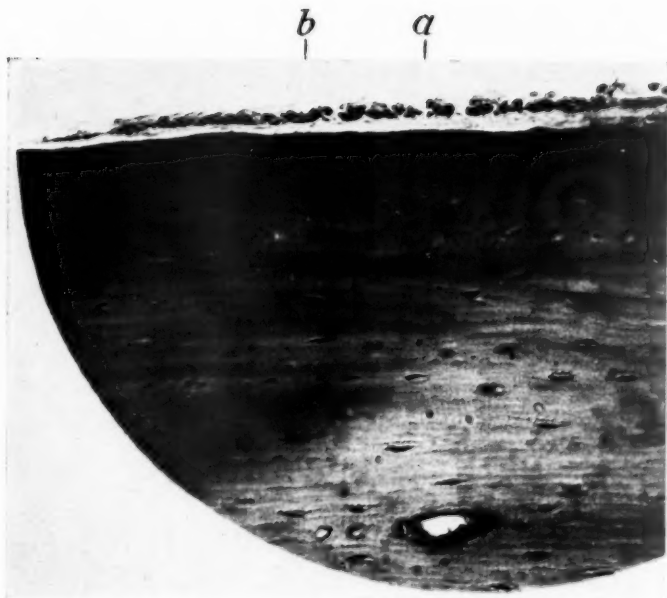


Fig. 19. A metatarsal bone from the experimental dog Lillemor before copulation. 270 times enlargement. A very thin layer of uncalcified bone (a) is noticed below the osteoblasts (b).

See p. 46, 47, 48, 49.

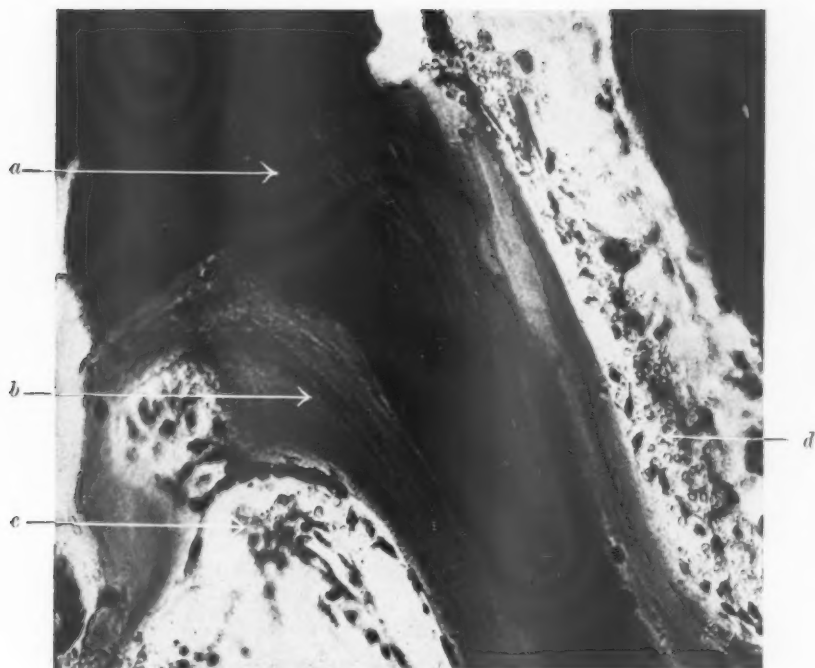


Fig. 20. A metatarsal bone from the experimental dog Lilleemor after the end of the lactation. 270 times enlargement. On the surface of the calcified bone (dark) (a) a broad layer of uncalcified dentin is noticed (b). The fat marrow has changed to an edematous fibrous marrow (c) where hemorrhages are noticed on some places (d).

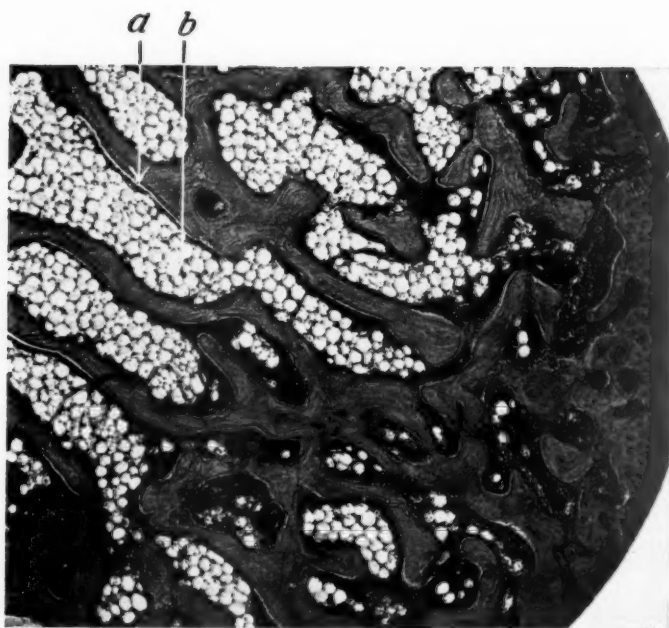


Fig. 21. Subchondral trabeculae from ulna in the control dog Lissen. 45 times enlargement. A very thin layer of uncalcified bone (a) is noticed on the surface of the trabeculae besides the osteoblasts. The marrow spaces are filled with fatty tissue (b).

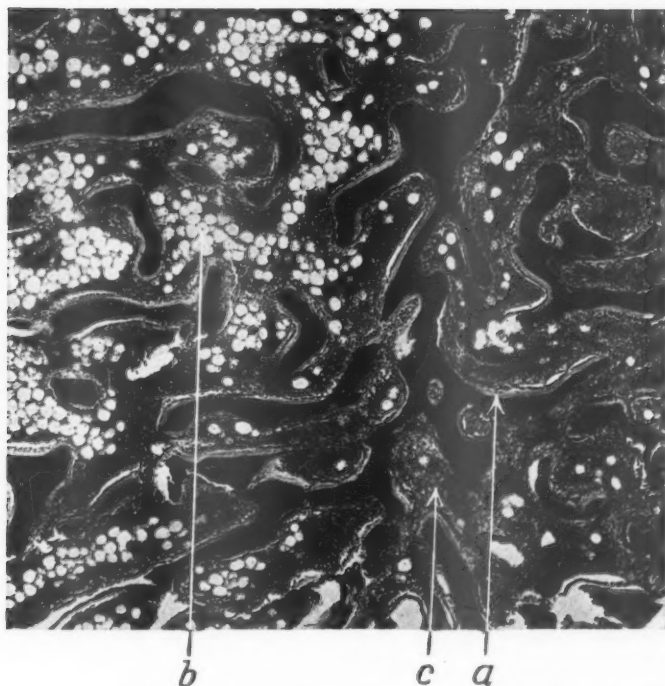


Fig. 22. Subchondral trabeculae from ulna from the experimental dog Siss, Ca, P and vitamin deficiency from the end of the lactation period. 45 times enlargement. A broad, light layer of uncalcified bone (a) is noticed, on the surface of which we may on some places differentiate the osteoblasts. The fatty tissue (b) of the bone marrow is on several places changed to a fibrous tissue (c). Here dilated vessels are noticed.

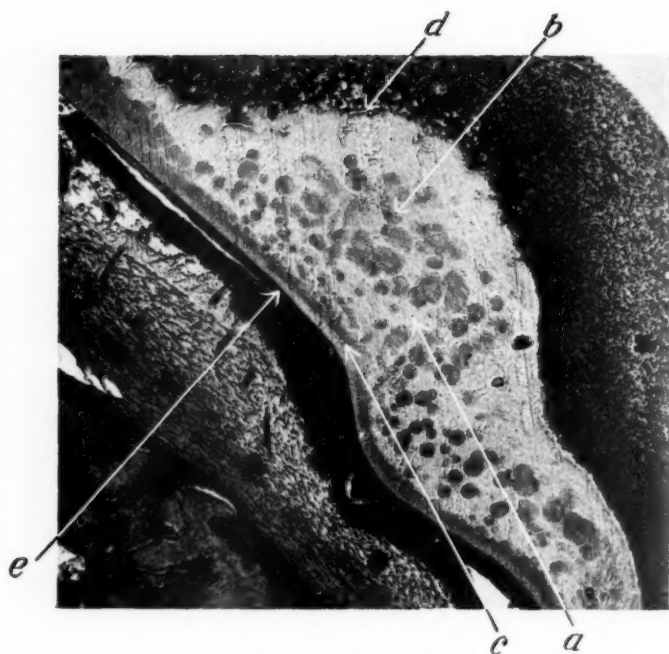


Fig. 23. A part of a tooth germ with surrounding jawbone from the experimental dog Grete: Ca, P and vitamin deficiency from the beginning of the lactation period. 45 times enlargement. In the broad uncalcified layer of dentin (a) round calcific globules (b) of varying sizes are seen. Towards the enamel a narrow stripe of calcified dentin (c) is noticed. The odontoblasts are unregularly arranged (d). The formation of enamel has just started (e). On the surface of the bone trabeculae broad, light uncalcified zones are found. The marrow consists of fibrous tissue.

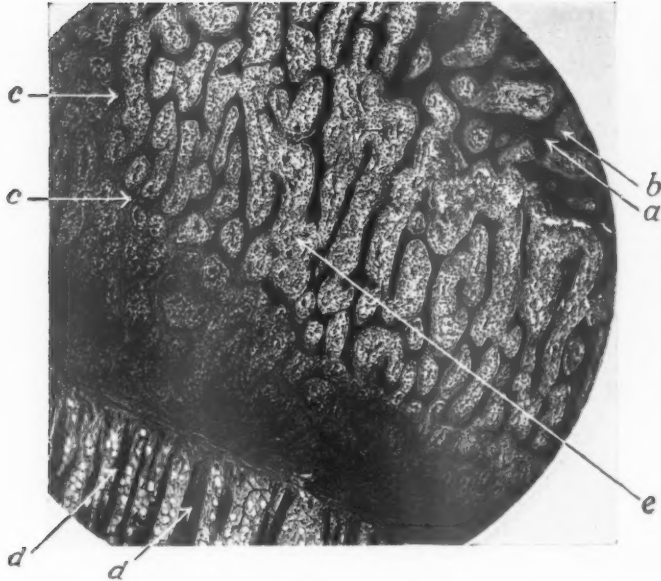


Fig. 24. Muscle insertion from an extremity from the experimental dog Eva: Ca, P and vitamin deficiency from the start of fetal life. 45 times enlargement. On the surface of the calcified trabeculae (dark) (a) we find light uncalcified zones of bone (b), on the surface of which osteoblasts may be found. Furthermore we notice completely uncalcified trabeculae (light) (c). The trabeculae are arranged according to the musclefibres (d), a functional arrangement. The marrow consists of fibrous tissue (e) and contains dilated vessels filled with blood.



Fig. 25. A microphotograph of a permanent premolar tooth from a normally fed puppy. We notice the thin layer of uncalcified dentin, indicated by an arrow, and the regular appearance of the calcified dentin.
70 times enlargement.

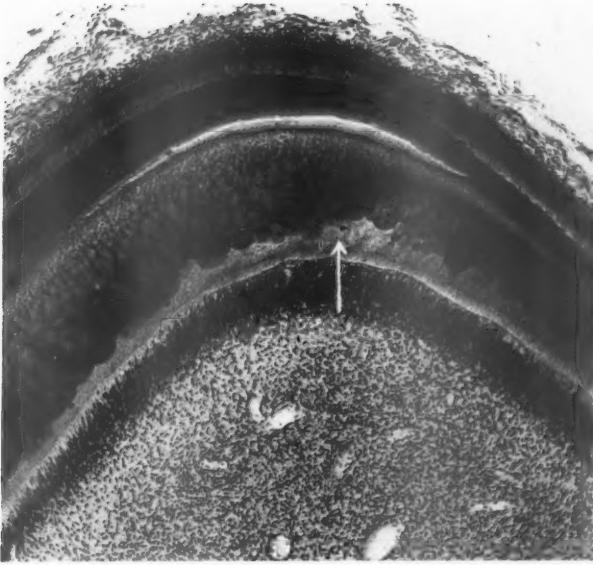


Fig. 26. A microphotograph of a corresponding tooth from Tell (Ca and P deficiency). Notice the broad layer of uncalcified dentin, indicated by an arrow. The dentin is irregularly calcified. Compare fig. 25.
70 times enlargement.

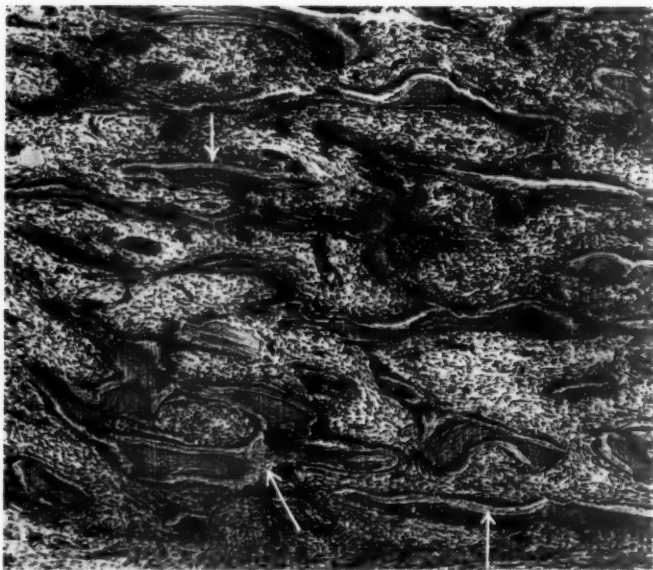


Fig. 27. A microphotograph of a rib from Tell (Ca and P deficiency during fetal and lactation period and later). 45 times enlargement. The picture demonstrates enlarged osteoid zones on the surface of the different bone trabeculae, indicated by arrows.

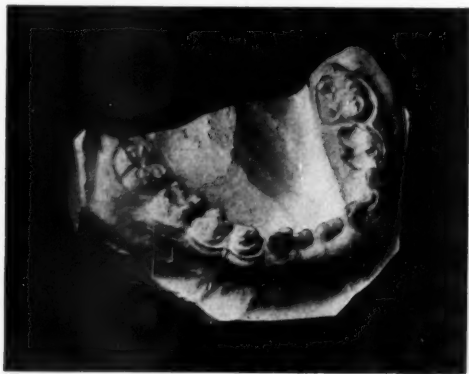


Fig. 28. A cast from the lower jaw of a 7 years old girl (E. S.) Gross hypoplasia of the enamel of all the temporary and the permanent teeth are seen. Decay in almost all indentations. Case history, see p. 97.

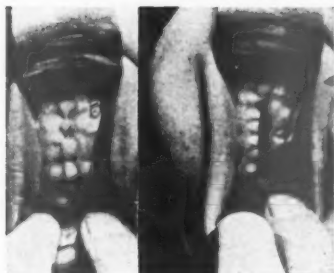


Fig. 29. A photograph of the frontteeth of Aa. S. (left) and H. S. (right) 7 and 6 years old respectively. Case history, see p. 98.



Fig. 30. A photograph of the frontteeth of H. N. 9 years old. Gross hypoplasia of the enamel with caries. Case history, see p. 100.



Fig. 31. A photograph of the frontteeth of G. O. 10 years old. The incisal part is relatively well calcified, but nearer the middle part of the crown marked hypoplasia are noticed. Extensive caries. Case history, see p. 100.

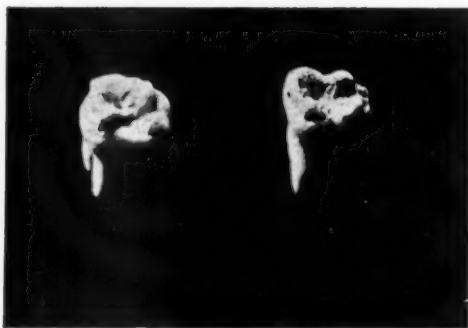


Fig. 32. A photograph of the six year molar from T. O. (6 $\frac{1}{2}$ year), to the left, and from E. B. (5 $\frac{3}{4}$ year), to the right. Gross hypoplasia are noticed with extensive caries and pulp involvement. Case history, see p. 101 and 102.



Fig. 33. A microphotograph of a ground specimen from E. B.'s molar. Microscopical hypoplasia are seen in the enamel as well as in the dentin. The enamel to the left and the dentin to the right.

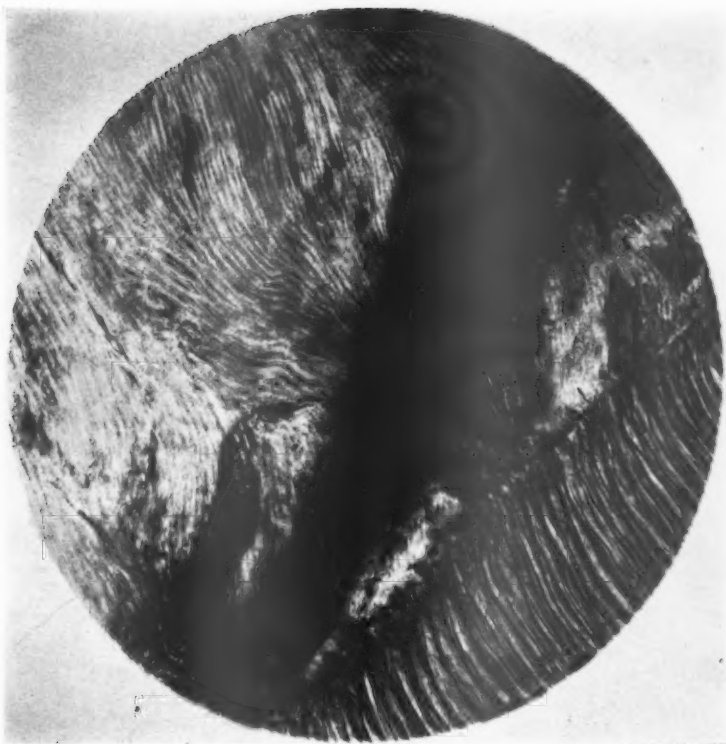


Fig. 34. Typical hypoplastic spots of the same tooth seen with higher magnification. The picture is not taken far enough into the dentin — down to the right on the picture — to show the interglobular spaces.

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THE DISTRIBUTION AND FREQUENCY
OF RICKETS IN ONE OF THE FISHERY
DISTRICTS OF FINMARK AND RELATION
OF DIET TO THE DISORDER

BY

JOHAN KLOSTER

Acta Pædiatrica. Vol. XII. Supplementum III

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Preface.

The present paper was in 1930 awarded the prize offered by the Medical Fund instituted by Messrs. The Freia Chocolate Factory, Ltd.

The work is founded on examinations made of 376 babies and infants, and 451 school children. The record sheets have, however, been left out, in order to save the expenses of printing.

All cases within the group of 376 younger children were carefully registered, each child being allotted a separate record sheet.

In these sheets the following particulars were recorded:
Essential facts and circumstances regarding the life of the child, race, extent of out-door life, general hygienic conditions at home, and, as far as possible, exact particulars in respect of the diet of the child itself, as well as that of the whole family.

The remaining entries give a sufficiently detailed account of the various examinations made, and the results obtained in each case.

In the case of school children, my materials include somewhat briefer general information, besides all particulars of positive rickets cases observed.

The judging committed consisted of Dr. med. CARL LOOFT, Bergen, and Professor Dr. med. THEODOR FRØLICH, Oslo.

The fact that my work, in its entirety, was accepted and approved by the Committee, inevitably includes an approval also of such parts of the materials as have had to be left unprinted,

from economical considerations. The guarantee thus afforded may, in a measure, serve to compensate for any incompleteness caused by the said omission.

In conclusion, I wish to express my most sincere thanks to my former chief, Dr. BJARNE SKOGSHOLM, district medical officer and hospital surgeon, for his great courtesy and unfailing goodwill throughout, by which he has in a very large measure contributed to facilitate my work in connection with the present paper.

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Introduction.

When commencing the present work of investigation, I quite realized that certain shortcomings would be unavoidable under existing circumstances. As this became no less clear to me during the subsequent working up of the materials collected, I propose, by way of a short introduction, to explain how these imperfections have arisen, and at the same time to point out such features of the case as have encouraged me to finish my paper and submit it to the judgment of the committee.

On January 1st 1928 I entered upon a situation as subordinate physician in one of the coastal districts of Finmark. The prize subject set for competition immediately caught my interest, and after some preliminary work — more especially as regards the acquiring of practice in estimating, in a fair and objective manner, the clinical symptoms of rickets — I started out to collect materials in March 1928.

The ideal plan would have been to make repeated examinations of a sufficiently large number of babies, say every three months, from birth until an age of two years, in order to observe and make note of all cases of rickets capable of being clinically diagnosed, as also for a better determination of climatic and dietetic influences. In the case of a so sparsely populated district as the one in question here, with about 150 births per annum, at least three years would be required to collect sufficient materials — even if no count be taken of the considerable distances (frequently 50 or 100 kilometres) to be covered in the collecting. Moreover, in order to be able to attend the children regularly, the visits would have

to be arranged according to a fixed plan or schedule, the carrying out of which would probably present very great difficulties even for the chief medical officer of the district himself, and certainly be quite impossible for one of his subordinates.

Instead of starting with a limited number of children, and subjecting single cases to a series of careful examinations, I have chosen to treat a larger number uniformly distributed over the whole of my district. By so doing I was able to examine the majority of infants at ages from a couple of months to two — five years, as well as most of the school children of the district, and also some children of ages between the two categories mentioned. My materials thus comprise 827 youngsters, all told, of which number 451 school children and 376 infants of more tender years. Most of the infants belonging to the latter group were examined twice, some of them several times, and but very few once only.

The above procedure may, no doubt, have allowed some light and transient cases of rickets, in year-old and two-year-old infants, to escape notice, as it will also have made it somewhat difficult to follow out and establish seasonal variations in the disorder.

I hope, however, that I have succeeded in drawing a true picture of the distribution and frequency of rickets within the district, and also think that the influences of diet on this disorder should be more readily ascertained with extensive materials than with narrowly limited ones, more especially as regards the consequences resulting from such differences of diet as must unavoidably exist in an extended district like the one we are at present concerned with.

At a cursory glance, the differences alluded to above might perhaps seem of but slight importance, but, nevertheless, I wish to point out at once that the district in question has to be considered as excellently suited for the study of dietic influences on rickets.

The desolate physical conditions of the coastal districts of Finmark reduce this population — isolated as it is from

the rest of the world — to a, practically, unvaried diet of fish.

Other matters, irrelevant to the subject on hand — or having only an indirect connection with it — have served to stimulate my interest still further, especially as regards investigations in this particular district. I am here referring to the fact that the district is situated in arctic regions, where the non-existence of rickets — as seen in connection with diet — was for a long time considered to be a fundamental truth. Of late years this axiom has been shaken, though the facts are as yet but little known. A contribution to the knowledge of rickets in these parts of the globe may therefore, possibly, lay claim to some especial interest.

A Description of the District.

My materials have been collected in the Vadsoe medical district, of which certain features have to be pointed out here — in conjunction with the map on p. 80 — as being essential for a proper understanding of the account given in the sequel.

The district is mainly situated on the north side of the Varanger fiord, and the whole of it lies north of 70° n. lat. The map also includes Bugöynes, a fishing hamlet situated in the South Varanger medical district.

The population of the district amounts to about 4,650 inhabitants belonging to 3 different races, *i. e.*: Norwegians, Quains (Finlanders), and Lapps.

Fishing being their chief means of subsistence, the inhabitants have settled close down by the sea shore, and in a manner which is typical of this district. As these settlements are frequently referred to in subsequent pages of the present work, a few descriptive remarks may not be out of place here.

The north coast of the Varanger fiord is entirely un-



Skallelv.



Salthjern.



Kiby.



Bugöynes.



Vadsoe.



Andersby.

sheltered by skerries, and the entrance of the fiord is quite open and exposed to the sea. Consequently, wherever a projecting cape, or an estuary, serves to suggest the makings of some kind of a harbour, people have flocked together and formed a fishing hamlet or »town», which latter appellation, being adopted from the Swedes, is commonly employed here.

Generally speaking, the population of any particular »town» consists of people belonging to the same race, and who have originally settled here at about the same time. In consequence they speak the same language, conform to the



V. Jacobselv.

same customs, and their conditions of living are also identical — in short, each hamlet may be, practically, considered as a collective unity. This fact has been of the greatest value to me, at all stages of the work in hand.

In most of the hamlets the race is pure and unmixed (*vide* markings on the map). With the Lapps the purity of the race is hard to determine; nevertheless, this part of the population may be said to form a special type apart. The three innermost hamlets I have marked as Lapp, and children of any mixed breed, not being essentially Lapp, have received a special note to that effect in my record sheets. — Hamlets inhabited by two different races are distinctly marked off on the map.

With the exception of some very few artisans, shopkeepers, and salaried functionaries, the population consists of fishermen, most of whom, beside the fishing, also cultivate some small holding, and keep a cow or two and a few sheep.

To supplement this brief description of the district I have, on pp. 8, 9 and 10, introduced some photographs showing how the »towns» are laid out. It will be seen that in every case the hamlet is situated on a projecting cape or near an estuary, and always quite close to the beach. The photographs will also give an idea as to the uniformity of architecture within each separate hamlet, whilst the same barren physical conditions are repeated in all of them.

Collecting of Materials. — Diagnosis.

Before passing on to a discussion of the actual materials, it may be expedient to put in a few remarks as regards the collecting of the same, and as to the importance I have assigned to any single symptom in its relation to the diagnosis and to the differential diagnosis.

My materials have been collected in the two-year period from March 1st 1928 to February 1st 1930. The majority of the 376 infants (children of less than school age) have been examined at their homes on my regular professional visits in the district, and also during leisure hours.

Owing to my being new and unknown in the district, all investigations were at first met with suspicion. This, however, gradually turned into confidence and goodwill, so that the work became steadily easier. One of the troubles to be reckoned with was the existing differences of language. This difficulty — combined with the too frequent absence of any faculty of observation on the part of the mothers — has led to my not daring to push my inquiries as far as might otherwise have been desirable, for fear of being misinformed. On the other hand I have always made sure, by

judicious cross-examination, that information received really was in conformity with the facts of the case.

The general course of my examinations I was able to gather from my record sheets, one of which had been allotted to each separate case, and information concerning diet was to be found endorsed on every sheet.

I have noted the time of eruption of first tooth and first ability to walk, without, however, attaching undue importance to these stages of the child's development in my diagnosis of each individual case.

It proved that while the rachitic infants included in my materials cut their first teeth at ages averaging upwards of $7\frac{1}{2}$ months, the corresponding average for non-rachitic ones was barely 7 months. With the rickety children the average age for commencing to walk was found to be slightly upwards of $13\frac{1}{2}$ months, as compared to slightly more than $11\frac{1}{2}$ months for the non-rachitic ones.

As the subjective element must necessarily enter into the appreciation of any particular symptom, and as some contention exists as to the importance of certain symptoms with regard to the diagnosis, I find it necessary to give an account of the rules I have gone by, chiefly in conformity with chapters VIII and X of the work by Dr. A. HESS.¹

The three symptoms given below I have considered as being pathognomonic for rickets, and whenever one or more of them were present, the child is characterized as rachitic (R+), no matter whether the disorder were active at the time or had left these traces only:

1) Craniotabes. — The characteristic yielding, like parchment, to the pressure of a finger on the parietal or on the occipital bone.

A certain softness in the bones of the cranium, and at the edges of sutures and fontanel, I have but accounted a

¹ »Rickets, Osteomalacia and Tetany.»

confirmation of a diagnosis principally based on other symptoms.

2) Rosary, or »beading» of the ribs. — In infants of any age between a couple of months up to a couple of years, I have accounted rachitic every fairly well defined rounded (not angular) protuberances at the junction of the ribs with the costal cartilages.

With the elder children, any somewhat more angular protuberances have been accounted rachitic as well.

3) Deformities of the thorax (»pigeon breast», Harrison's groove and flattening of the lateral curves of the ribs).

Wherever grave and protracted pulmonary affections have not existed early in life, I have noted the case as rickets positive (R+).

As regards the other symptoms, a certain graveness in the case of a single one, or the simultaneous presence of several of them, would be required to make me diagnose any case as R+.

A large head with an »Olympian front» and enlarged parietals and frontal bones, I have mostly accounted pathognomonic. An open fontanel at a later age than $1\frac{1}{2}$ years, enlarged parietal, a high palatal arch, irregular and badly enamelled teeth — each of these symptoms, taken singly by itself, I have considered as being in favour of the diagnosis, but a combination of two or more of them was always necessary to make me put down a case as R+. I have also taken the same view as regards abducted antebrachia, deformities of the spinal column, and genu valgum (Knock-knee).

An inconsiderable degree of bow-legs in a child, at about the age when it commences to walk, and not showing any other sign of rickets, I have characterized as R÷.

As regards the enlargement of the epiphyses, I have always had other symptoms in support of the diagnosis (whenever the above characteristic (R÷) has been employed).

Finally, I shall make brief mention of two of such differential diagnostic sources of error as ought to be especially kept in mind, *viz.*: Congenital syphilis, and Infantile scurvy.

The congenitally syphilitic child, with its large and angular head, and enlarged epiphyses, is liable to be considered rachitic. In the Vadsoe medical district syphilis is, however, a rare disease, and the existing sufficiently transparent social conditions make it easy to follow out and verify a case, when once it has been diagnosed. — In the case of one infant only, of all the 376, has there been some faint suspicion of congenital syphilis.

As far as infantile scurvy is concerned — having regard to the strict reservation observed in respect of angular protuberances, as mentioned above (*vide* »Rosary») — I think I have succeeded in reducing errors from this source to a minimum. This disease, or at least any distinctive case of it, is rarely met with in the Vadsoe district. — In the year 1929 only one case was diagnosed. — The fact that bottle-milk is hardly ever boiled may, perhaps, help to explain its rare occurrence in the district.

CHAPTER I.

The Distribution of Rickets in the District.

Throughout the whole district. — Of the 376 children examined, of ages from a couple of months to about seven years, 163 bore traces of rickets in their osseous system, that is to say 43,4 per cent. of the total number.

Of these 163 cases, I have characterised 27 as R + +, indicating that I consider them to be especially distinctive cases of rickets, who would be likely to carry evidences of the disorder beyond infancy.

Of the 451 school-children, of ages from seven to seventeen years, 60 showed traces of rickets in their osseous system, that is 13,3 per cent.

From the above figures it would appear that rickets is by no means a rare disease in the Vadsoe district, and also that especially distinctive cases may occur.

Within each hamlet. — From a consideration of the number of cases occurring in each of the hamlets, we may expect to acquire a fairly good general idea as to manner in which the disease is distributed throughout the district.

In table I (page 16) such numbers are given — for each hamlet — as will serve to illustrate the said distribution. These numbers are: The percentage of positive rickets, computed separately for infants and for school-children (columns 1 & 2), and the percentage of marked cases amongst infants (column 3).

From the table it appears that Skallelv occupies a peculiar position as regards the percentage of rickets, which is far in

Tabel I.

	Number of children below school age examined	Number of rachitic children	Percentage of rachitic children	Number of severe cases	Percentage of severe cases	Percentage of rachitic school children
Skallelv	41	30	73,2	10	24,4	31,3
Ekkeroy	13	8	61,5	0	0	8,6
V. Jacobselv	22	12	54,5	2	9	15
Golnes	34	16	47,1	4	11,8	14
Andersby	7	3	42,9	1	14,3	not ascert.
Vadsoe	129	53	41,1	9	7	10,3—20
Krampenes	11	4	36,4	0	0	11
Nesseby	53	19	35,8	1	1,9	9
Kiby	16	5	31,3	0	0	14,7
Bugoynes	33	10	30,3	1	3	not ascert.
Mortensnes	17	3	17,6	0	0	8,3
	376	163	43,4	28		

excess of that of any of the other hamlets. Although only one tenth part of the total number of infants examined belong to Skallelv, more than half of all the marked cases occur in this hamlet. Skallelv is, moreover, able to show the gravest of all the grave cases recorded.

The figures denoting the percentage of rickets, in infants as well as in children of school age, speak for themselves. A more vivid impression of the state of things here would have been acquired from a perusal of the 41 record sheets forming my register for Skallelv, but which — as mentioned in the Preface — unfortunately had to be left out of this work.

On page 17 I have introduced photographs of three cases, of which two were marked ones. Nos. I and II are of Borgny H., taken in the spring of 1929 and on January 10th 1930, respectively. No. III is of Erling N. (*vide* Examinations of

school-children in Skallelv). No. IV represents one of the milder cases.

The figures for the other hamlets also distinctly show



No. 1.



No. 2. E. and B. H., Skallelv 10/1 1930.



No. 3. E. N., Skallelv.

how very unevenly the disease is distributed throughout the district, the percentage differing as widely as from 61,5 for Ekkeroy to 17,6 for Mortensnes.



No. 4. Aa. E., Skallelv ¹²/₁ 1930.

By Curve I (p. 81) I have attempted to give a graphical representation of the distribution of the disease in this district. Andersby has been left out, on account of the few examinations made there. Two of the infants examined in this hamlet were born out of wedlock and have been badly neglected; they were both rachitic, one of them to a serious degree. The few school-children of the hamlet have not been examined.

We see that there is a certain degree of parallelism between the three curves. In the case of Ekkeroy there is, however, a considerable discrepancy between the percentage of rickets for infants and the two other percentages, both of which are seen to be pretty low. As this fact is not likely to be merely a matter of chance, I intend to make further reference to it later on.

Only a few features in connection with the »town»-wise distribution of rickets have been mentioned in this section, but in consideration of the importance of this subject to the present paper, I shall be frequently returning to it in subsequent pages.

Age. — The question of age, in its relation to rickets, being of especial interest, the figures in table II (p. 21) have

been arranged so as to show — separately for each of the eleven hamlets — the number of examinations made at various ages and the results obtained. The table also serves to facilitate comparisons with such results as may previously have been obtained by others.

From this table we arrive at the following totals respective of age:

Age (in years)	Total number of Examinations	Number of Positive Results	Percentage of Rickets
0— $\frac{1}{2}$	39	12	30,8
$\frac{1}{2}$ —1	61	27	44,3
1—2	106	53	50,0
2—3	81	33	40,7
3—4	55	21	38,2

At Skallelv, with the high percentage of rickets obtaining in that hamlet, a relatively large number of infants, at ages between 2 and 7 years, have been examined. The percentages of rickets are, moreover, exceptionally high there at these ages — right up to 68,9 per cent. If, for above reasons, the figures for all Skallelv children between 2 and 7 years of age are left out, the resulting numbers would be:

Age (in years)	Total numbers of Examinations	Numbers of Positive Results	Percentages of Rickets
0— $\frac{1}{2}$	39	12	30,8 (29,5)
$\frac{1}{2}$ —1	61	27	44,3 (66,1)
1—2	106	53	50,0 (63,6)
2—3	72	26	36,1 (38,2)
3—4	45	15	33,3 (31,5)
4—7	42	13	31,0 (9,5)
			(anything above 4 years)

For the sake of comparison, I have placed Professor A. JOHANNESSEN'S¹ percentages (in brackets) side by side with my own. According to my records, the climax occurs between the ages of 1 and 2 years, which is one stage later than found by Prof. JOHANNESSEN. (According to the latter, Professor COHN has found the highest percentage of rickets at ages between one and two years.) Whilst my highest percentage is 50, Prof. JOHANNESSEN has arrived at a maximum of 66,1 per cent. To some extent, at least, this difference may be due to the fact that Prof. JOHANNESSEN'S data were collected exclusively from ailing children, whilst, on the other hand, medical assistance was called for in but very few of my cases. Taking this into consideration, it may well be that the difference is not in reality as large as appears from the two sets of figures given for the youngest ages, and having reference to conditions in the north and the south of Norway, respectively.

However, there is probably not much to be gained by carrying such comparisons too far. As mentioned above, Prof. A. JOHANNESSEN'S materials apply to ailing children; they were collected years earlier than mine, and also in quite a different manner. — Before leaving this subject, I find it necessary to call attention to the percentages given for ages above 4 years, where the figures are seen to differ to a considerable extent — 31 per cent. as against (9,5 per cent.). If this large difference be real, it will hardly do to pass over it without any remark. It should be noted that Professor JOHANNESSEN'S figure (9,6 per cent.) applies to any age above 4 years — there being no upper limit — whilst the 31 per cent. found by me have reference only to children up to 7 years of age. In this connection I wish to mention a circumstance that may, to some extent, have served to raise my percentage, namely, that it was my invariable habit, whenever the youngest infants of a family proved to be distinctively rachitic, also to examine the elder ones who were then very often found to have been suffering from rickets as well. On the other hand, although this practice of mine does not affect children of school age,

¹ Prof. A. JOHANNESSEN: »Bidrag til Studiet av Rachit».

Table II.

Age (years)	Skallieiv		Ekkeroy		V. Jacobselv		Golnes		Andersby		Vadsø		Krampenes		Nesseby		Kiby		Bugøynes		Mortensnes	
	R-	R+	R-	R+	R-	R+	R-	R+	R-	R+	R-	R+	R-	R+	R-	R+	R-	R+	R-	R+	R-	R+
$\frac{1}{2}$	0	3	0	0	1	1	7	1	0	0	16	5	0	0	3	2	0	0	0	0	0	0
1	1	3	1	1	2	1	0	4	0	1	18	11	2	0	5	6	0	0	0	0	5	0
2	3	7	4	5	0	7	7	4	1	0	20	19	1	0	8	6	2	1	5	3	2	1
3	2	7	2	2	6	2	3	3	0	0	10	13	3	2	10	2	3	0	7	2	2	0
4	4	6	2	0	1	1	2	2	1	0	4	4	1	2	4	2	4	0	8	4	3	0
7	3	7	0	0	0	0	1	1	2	2	10	0	1	0	8	4	2	3	3	1	2	2

my percentage for such children is nevertheless higher than that found by Prof. JOHANNESSEN, the figures being 13,3 and 9,5 per cent., respectively.

As matters stand at present, it may be hard to determine whether the figures 31 and 9,5 really express the true percentages. It is not unthinkable that the long and dark winters may cause the disease to remain active through a longer period, or at least to leave more distinct traces, than what would be generally the case in lower latitudes.

In connection with the above, it may not be inappropriate to give a thought to rachitis tarda. I can only say that I have not met with a single case of late rickets; nor have I ever been able to record active rickets at a later age than two years. Nevertheless, I should not like to give an opinion on this last mentioned subject.

Heredity. — In connection with what has been mentioned in a previous section with regard to families of rachitic children, I am now going to touch upon the question of heredity, in so far as my materials may be said to have any bearing on the subject. This discussion must of a necessity be very brief, owing to the entire unwillingness on the part of the adults to submit to any kind of examination. — Particularly at Skallelv, I often attempted to make such examinations, one of the reasons being that I wished to form some sort of an opinion as regards rickets in the generation which had at the time arrived at the grown-up age — but it invariably proved quite impossible to make the parents catch on to the idea. Consequently I have had to be satisfied with whatever information I was able to get in other ways.

At Skallelv there are three brothers H. living — Ludvig, Victor, and Oscar — all three married. As children these brothers were so decidedly bow-legged that they had to be nicknamed accordingly.

Examinations of three of Ludvig's children were recorded as follows: Alf Erling R + + +, Ivar Simon R + +, and Henry R +.

Victor's children: Aksel Erhardt R+, Borgny R+++ , Thorolf Aasmund R-, and Ewald R+. — Some time ago Thorolf Aasmund had been very bow-legged, and this was now the case with Borgny and with Ewald as well. It looks as if bow legs were hereditary in this family.

For Oscar's children the results are: Frantz Odin R+++ , Alice R-, and Gunwald Th. R+++ .

At Little Salttjern (Golnes) the boy Martin Godfred H. and his two sisters were entered as R+++ , R+, and R+, respectively. A paternal uncle of these children is said to be distinctly pigeon-breasted.

At Hoivik the two brothers Hilmar and Hjalmar D. were both entered as R+. The father of these children is distinctly pigeon-breasted.

Aldrik Viliam J. and his three brothers and sisters have R+++ , R+, and R+, respectively. The paternal grandfather of these children who lives in Finland is decidedly pigeon-breasted, and their father distinctly bow-legged.

Above are given the cases in which I succeeded in getting information as to heredity, besides those that are mentioned at the end of the section. Of 18 children examined 16 are rachitic, that is to say 88,9 per cent., and 7 of the 16 rickety infants are severe cases. In all these cases we find external causes which may serve to explain a high percentage of rickets; but the actual magnitude of this percentage — which decidedly outdistances that of Skallelv — seems to suggest the presence of some especial element. I am here alluding to a constitutional factor; the hereditary disposition. This subject is also touched upon in the section on Race and Rickets.

A great authority, Dr. A. HESS, does not consider the above constitutional factor as being of predominant importance in connection with the origin of rickets.

From the scant information which I have to go upon, I have received the impression that the constitutional hereditary factor is not to be dis-regarded, as far as my materials are concerned. I have to admit, however, that I have not tried for information as to the prevalence of rickets in a family,

excepting in cases where the flock of children were distinctively rachitic.

In connection with the question of pelvic deformity I have tried to trace rickets in the mothers of the children included in my materials. In 34 cases, or 5.6 per cent., of the 612 births occurring in the town of Vadsoe (1917 to 1928), surgical operations were necessary, not counting afterbirth operations.

Of these 34 women, 3 are mothers of children included in my materials, viz.: Magna V., Amanda B., and Aud W., the children of whom have R÷, R+, and R+, respectively.

Two of the women were delivered by forceps, and one, Amanda B., by the Cesarean operation; it is quite certain that the latter has a deformed pelvis.

In the North Varanger country district, from Skallelv to Jakobselv (both included), 203 childbirths occurred during the period 1912—1925, out of which surgical operations were necessary in 5 cases, or in 1.7 per cent. of the total number. In a large measure this low percentage is due to the long distances from doctor and midwife.

One of the five women mentioned above was the mother of Gunvor H. (*vide* the Childrens' Home Vadsoe). She was a dwarf, and the Cesarean operation became necessary.

At Skallelv, with about 10 childbirths per annum, surgical operations were necessary in 2 cases, or 1 per cent, which seems to indicate that rickets may have been a not very common disease with the mothers of the present Skallelv-generation, most of which women were themselves born in that hamlet.

For the sake of comparison with the above obstetric data, I may mention — from the Annual Medical Report of Norway, 1916, — that out of the 54,121 childbirths occurring in this country, surgical operations (not including secundine operations) were performed in 2,776 cases, which works out at 5.13 per cent. In so far as a comparison between the above percentages be permissible, the Vadsoe district does not appear to differ in any marked degree from the rest of the country in

respect of the prevalence of pelvic deformity if we may count this indication a dominating cause for surgical delivery operations.

Race and Rickets. — This subject may be treated of in connection with the question of heredity. During the collecting of materials I very soon received the impression that rickets seemed to be less prevalent with the Lap's part of the population than amongst the Quains.

Of the 53 children belonging to Nesseby (Karlebotten, Sirdergope, Vesterelv and Nesseby) 9 were not Lapps, and of the remaining 44 children 14 or 31,8 per cent. — were rickety. Only one of the cases has been entered as R++.

Of the 129 Vadsoe children 60 are Quains, with 25 cases of rickets, of which 5 are R++.

45 children are Norwegian, with 16 cases of rickets of which 1 R++.

1 child was a Lapp, and 23 children were of mixed breed.

I have below arranged the children according to race, and given the number and percentage of rickets cases for each of the three races, separately.

Quain Children below school age.

	Number of Infants examined	Number of Cases
Skallelv	41	30
V. Jacobselv	22	12
Golnes	34	16
Vadsoe	60	25
Bugeynes	33	10
	190	93

Of the Quain children 49 per cent. are rachitic. Out of the 190, 22 children were marked cases, that is to say 11,6 per cent.

Norwegian Children below school age.

	Number of Infants examined	Number of Cases
Ekkeroy	13	8
Andersby	7	3
Vadsoe	45	16
Kiby	16	5
Mortensnes	17	3
	98	35

Of the Norwegian children 35,7 per cent. are rachitic. Out of the 98 examined, two children, or 2 per cent., were marked cases.

Lapp Children.

Nesseby	44	14
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Of the Lapp infants 31,8 per cent. are rachitic. One child out of the 44 was a severe case, that is 2,3 per cent.

There is thus a marked difference between the three races as regards the frequency of rachitis — at all events between the Quains and the Lapps, the larger percentage and the graver cases being with the Quains.

This difference must be ascribed, either to existing external conditions, to habits of life, or to a constitutional factor.

With regard to frequency of rickets, the Norwegians have to be placed somewhere between the two other races, and in Vadsoe — where the external conditions are more equal — very close to the Quain race. This circumstance, and the fact that any small difference between the Norwegian and the Quain part of the population may be entirely due to different external conditions, are strongly in disfavour of attaching importance to the influence of inherent racial qualities — at least as far as the two latter races are concerned. In speaking of different external conditions I allude to the fact that of

the Quain infants in Vadsoe only 15 — or 25 per cent. — were breast-fed, as against 66,7 per cent. of the Norwegian babies. With this statement I am anticipating the question of breast-feeding *versus* bottle-feeding, and it may as well be added at once that my materials speak strongly in favour of breast-fed infants.

As the said materials furthermore show that 65,2 per cent. of all the Norwegian infants included were breast-fed — against 37,4 per cent. of the Quain infants — and also evidence a similar difference in favour of the Norwegian children with regard to out-door life, it would perhaps seem somewhat far-fetched to look to inherent racial qualities for an explanation of the differing frequencies of rachitis in the two races — the more so, as Dr. A. HESS does not ascribe any predominant importance to those same qualities.

This becomes less plain in the case of a comparison between the Quains and the Lapps. Of all the Lapp infants included in my materials, 27 — or 38,6 per cent. — were breast-fed, as against 37,4 per cent of the Quain infants, whilst the amount of out-door life comes to about the same thing in either case (*vide* p. 32). As there is, nevertheless, a marked difference as regards the frequency of rickets in the two races, it seems very difficult flatly to deny the possible existence of some constitutional factor tending to manifest itself as a less pronounced predisposition for the disorder in the Lapp race than in the Quain. However, in the chapter on nutrition, and in connection with a discussion on the effect of vitamines on the frequency of rickets in the two races, I have shown that the diet of the Lapps ensures a richer supply of vitamines than does that of the Quains.

I am not here intending to subject the question of racial influences to a discussion in all its bearings, but only sufficiently to clear the way for a discussion on the influence of diet. Nor does the extent of my materials allow of any discussion of the former kind, as they include Lapps and Quains from within very limited precincts.

In a letter of October 29th 1929 Professor K. SCHREINER

has kindly replied to my enquiry as to traces of rickets to be found in the university's collection of Lapp skeletons. I beg to quote a fragment of this letter, translated into English: »— — — it is certain, however, that among the Lapp skeletons included in the collection of the institute not few examples of rachitic deformities are to be found. Among the Lapps in Tyssfjord I have myself had occasion to observe alterations in the skeleton, which I thought had to be considered as being of a rachitic nature.»

In view of the statement cited above, we may perhaps be justified in regarding inherent racial qualities as being of less importance, in this connection, than certain external circumstances, more particularly the effects of diet dealt with in subsequent pages of the present work (*vide*: The Discussion, Chapter II).

The two Sexes. — The total of 376 children below school age comprises 193 male infants of which 110 (or 57 per cent.) affected with rickets, and 183 female infants of which 54 (or 30 per cent.) are rachitic.

Professor A. JOHANNESSEN has arrived at a less difference in the percentages, 56,9 per cent. of his boys and 43,1 per cent. of his girls being rachitic. According to the same authority, Dr. QUSLING had 59,1 per cent. and 40,9 per cent., respectively for boys and girls, and Dr. C. LOOFT a still wider difference, the largest percentage being on the male side.

In all of the examinations made of Norwegian children, as stated by Professor A. JOHANNESSEN, the preponderance of rickets in male infants is evident, contrary to the results published by several foreign authors. Neither does Professor A. HESS formulate any fixed standpoint as to the differing propensity for rickets in the two sexes, though he refers to Dr. FROMME's assertion that the ratio of rachitis tarda, in male and female individuals, is as 15 to 1, respectively.

Out of my total of 451 school children, the sex is specified in 381 cases. Of this latter number 177 are boys, including 41 (or 23,2 per cent.) affected with rickets, and 204

girls, including 15 (or 7,4 per cent.) affected with the disorder. The proportion which the number of male rachitic children bears to the female ones is seen to be further increased from 2 to 1 in infants, to 3 to 1 in school children. In order to ascertain whether or not this difference might continue decreasing with the lower ages, I have gone into the matter in the case of infants below the age of 2 years, and have found the proportionate number to be as 2 to 1.

With a view to ascertain to what extent sex may possibly have any bearing on the percentage of rickets in each particular hamlet, I have here below appended the proportional of boys (below school age) to the total number of children of both sexes examined, for each of the 11 hamlets, separately:

Skallelv	60	per cent.
Ekkeroy	61	" "
Jacobselv	54,5	" "
Golnes	50	" "
Vadsoe	55	" "
Krampenes	50	" "
Nesseby	54,7	" "
Kiby	43,8	" "
Bugoynes	42,5	" "
Mortensnes	30	" "

The greatest difference in the apportionment of the two sexes is found between Mortensnes and Ekkeroy. Therefore, in order to enable us to draw a comparison between these two hamlets, we have to imagine an addition of 5 boys to the number actually examined in Mortensnes, and, further, to assume that 1 of the additional boys (or 20 per cent.) be rickety. We may then reasonably conclude that the sex factor does not appear to be of material importance, neither in Mortensnes nor in any of the other hamlets, as far as the »town»-wise distribution of rickets is concerned.

In the case of the school children included in my materials, the greatest difference appears between Skallelv and Golnes, the percentages of boys examined in the two places

being 56,3 and 36,7, respectively, which makes a difference of about 20 per cent. Thus the latter hamlet has a deficiency of 8 boys as compared to the former. At Golnes the percentage of rickets in boys is 27,8, and in girls it is 6,5 per cent. If we assume a percentage of $27,8 - 6,5 = 21,3$ in the above-mentioned 8 boys, then this would make an addition of 1 to 2 rachitic boys to the original 7, and fix the percentage of rickets in Golnes at between 16,3 and 18.

In spite of the above correction, Skallelv proves to maintain her position as the hamlet having by far the largest percentage of rachitic children.

I may also add that among the Skallelv children examined the higher percentage of rickets is with the girls, the percentages being 33,3 for girls and 31,3 for boys.

In the case of the other hamlets the two sexes are more equally apportioned, so that the sex factor becomes of even less effect.

Out-of-door Life. — Only a very small minority of the population of this district have any idea as to the beneficial influences of light and fresh air. Even in cases where the open air is not considered to be directly injurious to infants, the parents do not make a special point of seeing that the children regularly receive the benefits of staying out-door for some time every day. This matter is generally limited to some warm days when the mother, or a sister, is at liberty to look after the child for a while. Thus the children are frequently taken along into the fields in the hay-making season. The fact that the extent of children's out-door life is largely governed by chance has not failed to affect the degree of completeness as to the information I was able to gather on the subject.

In my investigations I have touched upon the age at which the child was taken out-doors for any appreciable part of the day, and I have otherwise tried to get information of particulars that might be of interest with regard to the pre-

sent subject. I recorded the answers that seemed to be consistent and unequivocal.

The majority of nurslings, as well as of infants below the age of two years, are taken outdoors in June, more extensively in July, August, and during part of September as well. But very few infants are taken out during the remaining 8—9 months. Taking this circumstance into consideration, the grouping in Table III virtually divides the children into »Spring children» (those that were born in the spring) and »Autumn children» (those born in the autumn).

Group I (V.: Table III): This group comprises the children who have had an appreciable out-door existence during the first half year of their lives. Most of the children in this group are »Spring children».

Group II: Children who have led an appreciable out-door existence during the first year. Most children in this group are »Autumn children».

Group III: Children who have not had an appreciable out-door existence in the course of the first year of life. »Spring children» and »Autumn children» are both to be found in this group.

The percentages of rickets in these three groups show the distinctly beneficial effect of an extensive out-door existence.

Group I: The percentage of rickets is 32,8

» II: » » » » 49,1

» III: » » » » 60,8

In order to acquire a more comprehensive idea as to the effects of an extensive out-door existence within each particular hamlet, I have, in Table IV, page 34 joined groups II & III under the common heading »Little out-of-doors», in contradistinction to group I, »Much out-of-doors». I have, furthermore, computed the percentage of »little out-of-door» children for each separate hamlet, though I am, of course, aware that this matter cannot be exactly expressed in figures.

Taken in conjunction with the impression received from working on this subject, I do not think that the given percentages in any way tend to convey a misconception of the actual facts. It is in the case of Skallelv only, that I might feel inclined — after having conferred with the school master of that hamlet, and with the chairman of the local nursing society — to raise the percentage, bringing it closer to the figure for Golnes.

Putting the percentage figures into words, we may briefly say:

In *Skallelv* and *Golnes* only a minority of the »spring children», and about half the number of »autumn children» are taken out-doors during the first summer of their lives. — In *Bugoynes* many of the »spring children» and most of the »autumn children» are taken out doors during the first summer. — In *Jacobselv* these conditions are even somewhat more favourable, inasmuch as the spring season is also taken advantage of in some cases.

Nesseby may be likened to *Jacobselv*. When Lapp children have become a couple of years old, they are probably taken somewhat more frequently out-doors than other children of the district, well dressed as they are in their reindeer-skin or sheep-skin clothes. The same thing may perhaps be said of the Lapp women as well, which may be of some interest for the purposes of this paper, in so far as the pregnant women and the nursing mothers are concerned.

In *Vadsoe* and, in the hamlets inhabited by Norwegians, the conditions are somewhat better still, *Vadsoe* and *Mortensnes* being the two most favourably situated places in this respect — An exception has to be made in the case of *Ekkeroy*, however, as this hamlet compares best with *Nesseby*.

As we have seen, the Quain and the Lapp part of the population are behind the Norwegians of the district, in so far as out-door life of infants is concerned. This circumstance must be seen in connection with the higher degree of isolation of the two former races. They are but slightly in touch with physician and, especially with qualified midwife, and con-

sequently ignorant of modern infant hygienics. In these hamlets, unlicensed local accoucheuses still deliver most of the women in childbed and, conjointly with the old people of the family, direct the tending of the child, which results in a horror of fresh air, and leads to an extensive bringing up by hand. — The fact that Ekkeroy is the only hamlet inhabited by Norwegians, where a similar accoucheuse is generally employed, falls well into line with what has been stated above, concerning this hamlet — a circumstance to be borne in mind later on, when the question of breast *versus* feeding-bottle is being discussed.

Thus, the beneficial effects apparent in connection with »much out-of-doors» are not wholly due to an appreciable out-door existence by itself alone. In conjunction with the unfavourable effects of »little out-of-doors», the undesirable consequences of bottle-feeding have to be considered as well. Out of the 51 infants in group III, Table III, as many as 32 have not been suckled — that is to say 62,7 per cent., as against 45,7 per cent. when calculated from the total numbers included in my materials, being 172 infants out of 376.

Seasonal Effects. — In order to acquire some idea as to how the seasons of the year might affect my materials, I have — in Table V — arranged the numbers of examinations of infants below the age of two years, according to the months in which the examinations were made, and according to the results of the diagnoses. As will appear from the table, there are, unfortunately, very few examinations in June, July, August, and September (my time being occupied with having to act as substitute for others during those months). However, if the examinations made in those 4 months be added together, it gives us 12 examinations in all, with 3 positive rickets cases, or 25 per cent.

In my materials, the month of April gives the highest percentage of rickets, and the summer months give the lowest figures. It must be considered, however, that the number of examinations is low — and even if we, *a priori*, and parti-

Table III.

	Group I		Group II		Group III	
	R—	R+	R—	R+	R—	R+
Skallelv	2	3	4	7	3	8
Ekkeroy	4	2	0	4	1	2
V. Jacobselv	6	1	3	7	1	3
Golnes	1	0	8	10	5	6
Andersby	2	1	2	2	0	0
Vadsoe	46	31	15	14	5	4
Krampenes	1	1	3	0	1	0
Nesseby	11	3	10	3	2	5
Kiby	5	2	5	2	0	0
Bugoynes	4	0	6	4	1	2
Mortensnes	8	0	1	2	1	1
	90	44	57	55	20	31
	134		112		51	

Table IV.

	Group I	Groups II & III	Percentages of »Little Out-of- Doors» Infants
Skallelv	5	22	81,5
Ekkeroy	6	7	53,8
V. Jacobselv	7	14	66,7
Golnes	1	29	96,7
Andersby	3	4	57,1
Vadsoe	77	38	33,0
Krampenes	2	4	66,7
Nesseby	14	20	58,8
Kiby	7	7	50,0
Bugoynes	4	13	76,5
Mortensnes	8	5	38,5

Table V.

	Total Numbers of Examinations	Cases of Rachi- tis positive	Percentages of Rachitis +
January	117	48	41
February	27	9	33,3
March	16	11	68,8
April	11	8	72,7
May	13	7	53,8
June	3	2	25,0
July	4	1	
August	3	0	
September	2	0	
October	59	19	32,2
November	65	26	40,0
December	22	7	31,8

cularly in Finmark, might expect to see strong seasonal fluctuations in the percentages of rickets, nevertheless, the 72,7 per cent. for April, as against 25 per cent. for the four summer months, seems to be a pretty considerable jump. Still, my figures serve to show — in a general way, at least — that the cases increase in number in the course of spring, decrease rapidly during the summer months, and retain a relatively low number in the course of autumn and winter. This seems to agree quite well with what has been previously stated respecting the beneficial effects of out-door life, the infants being most frequently taken out during the summer months. This circumstance, and the sunlight's relative richness in ultra-violet rays in these latitudes, on one hand — with the extremely dark and very cold winter, on the other hand — may seem to indicate that the figures I have given probably cannot be very far out.

The fact that Dr. A. RASMUSSEN has not in the Faroe Islands observed any strong seasonal fluctuations in the frequency of rickets (craniotabes) may possibly be due to the

hazy atmosphere prevailing in those parts, and to the comparatively slight variations in the general character of the different seasons. He states, however, that the disorder most frequently commences during the period November to May. — Professor A. JOHANNESSEN gives the preponderating number for the months from April to June. According to this same author, Dr. QUISLING has observed the majority of cases in the summer months, while Dr. C. LOOFT has experienced the fewest cases in January and in September (3,2 per cent.), and the highest number in June (16,3 per cent.).

Finally, if we consider the seasons at which examinations have been made in each of the hamlets — with a view to ascertain whether this might perhaps have a disturbing effect as regards the percentage of rickets given for any single hamlet, relatively to the percentages given for the other hamlets — we see (table not printed) that such consideration may be of interest in the case of Nesseby and Skallelv, only. The examinations in April and May have had the effects of unduly raising the percentage for Nesseby a little, and that for Skallelv a trifle.

Conditions of Climate. — In connection with the two previous chapters, it may be of interest to consider a few of the climatic conditions.

The climate of the district approaches to an inland climate, with inconsiderable precipitation. The winters are long and severe, and even though the temperature does not sink far below zero (the freezing point), the cold is keenly felt, on account of the continual, strong winds. It is easily comprehensible that women and children keep indoors during the greater part of the winter. Summers are short, comprising the months of July and August; but June and September also usually prove to be decently fair, in part. The summers of 1928 and 1929 were poor, with no proper summer temperatures. The summers of 1924 and 1926, with weeks on end of sunshine from a clear sky, would compare favourably with

the finest summers in the south of Norway, as far as summer-heats are concerned.

For the Vadsoe district proper, there are no officially published meteorological data. Below, I shall quote some figures from Professor AMUND HELLAND's book »Norges land og folk» (»Country and People of Norway»). This author speaks of »sea stations» and »fiord stations». With regard to climate, the Vadsoe district may be said to occupy an intermediate position between the two, the conditions in the eastern parts of the district approaching more closely to those of the »sea stations», and in the western parts to those of the »fiord stations».

According to prof. HELLAND, the mean annual temperature lies between $0^{\circ},6$ and 2° C. at the sea stations, and between $0^{\circ},5$ and $0^{\circ},8$ at the fiord stations. The lowest temperature in winter lies between $3^{\circ},5$ below zero and $6^{\circ},4$ below (on centigrade scale) at the former stations, and $7^{\circ},5$ to 12° below zero at the latter stations. In return, the summer months are somewhat colder at the sea stations. The precipitation is small, practically the same for the whole district, about 600 mm. per annum.

There is no difference in the general character of the climate of the inner (western) part of the district and that of the outer (eastern) part. Winters are equally severe in all parts, and in summer the difference in the number of bright days at Skallelv and at Karlebotten is by no means particularly striking. It must be admitted, however, that a hot summer day is hotter at the latter place.

From about November 20th to about January 20th the sun is not seen. During this period of obscuration the children generally grow pale, without, however, suffering any change as to general health. In the record sheets of children that were examined in the course of these and the two contiguous months, I have often made the entry »pale complexion», merely for a memorandum of their appearance at the time, and not to express any observed lowering of vitality. Only very few children — at least as compared to the great many

who grow pale — suffer from insomnia, or lose their appetites, during this period. Cases of such disorders have invariably been entered in the record sheet of the child concerned.

From the period of obscuration to lighter days, the transition is very rapid, but generally accompanied by more cold weather, so that an almost wintry atmosphere is frequently experienced until well into the month of May. Nevertheless, it is especially during the spring season that occasional splendidly clear days occur — resembling Easter days on the high mountains in the south of the country — with bright sunshine from a cloudless sky, and dazzling reflexions from the snow-covered hills and plains, and from the glassy surface of the fiord.

The midnight sun is visible from about May 17th to about July 25th, and there are, practically, no mountains to obstruct its rays.

In June a few summer days generally occur, in which the children are allowed outdoors, July and August are the summer months proper, and September may be a good month, too. However, in the autumn of 1928 the snow came in the middle of September, and remained for good.

By the courtesy of a private gentleman I have had an opportunity to examine his careful and exact notes on the weather for the past two years.

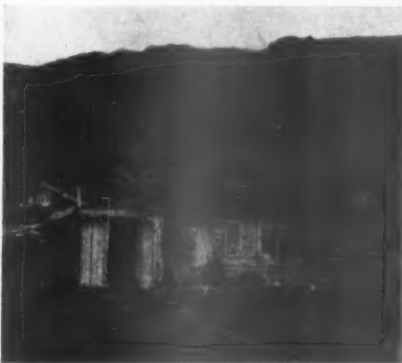
I append the following figures concerning the last two summers:

Out of the 122 days of June, July, August, and September 1928, there were 47 days with considerable sunshine, 18 days were dim (haze, overcast sky, rain), the remaining 57 days were without any sunshine to speak of, but also without any haze.

For 1929 the figures are: 31 bright days, 33 hazy, and 58 of no especially marked character.

In spite of the particularly sunless summer of 1929, a physician, returning from a holiday trip to more southern parts, expressed his astonishment at the fine, tanned complexion of the youngsters here, as compared to his impressions from the south of Norway.

In conclusion, I wish to make mention of a thing that appears to be of some importance in this connection, *viz.*: Mr. OTTO KESTNER's measurements of the biologically effective, short-wave sunrays, at two stations situated north of the Arctic circle (Abisko and Svolvær, August 1926). He showed that there proved to a considerably larger quantity of such rays at the above two places than — at corresponding altitudes of the sun — to be found in the Temperate Zones. I have barely alluded to this circumstance in the section on Seasonal Effects, where it is indicated that the considerable reduction in the percentage of rickets, during the summer months, may probably be partly due to the rays in question, and also that the distinct effects of outdoor life (mostly lead during the summer) may likewise be partly ascribed to the same source.



Lapp dwelling.

Habitations. Cleanliness. — These two factors can hardly be said to figure very largely in modern investigations of rickets. Whoever might concern himself in such investigations, in the Vadsø district, would very soon agree to this statement.

The Lapp part of the population — in spite of their small, badly ventilated and stuffy cabins, and their want of cleanliness — suffer considerably less from rickets than do the Quains, with their larger and better ventilated dwellings, and higher degree of cleanliness. We find the highest percentage of rickets at Skallelv, as well as the most satisfactory habitations.

When I am, nevertheless, going to touch on these hygienic subjects, it is because, in so doing, I shall be conveying an idea as to the peculiar life-conditions of this population.



Lapp dwelling.



Lapp dwelling. Mud Hut, Nesseby.



Lapp dwelling. Nesseby 29/11 1929.



Lapp dwelling. Mud Hut, Nesseby 19/1 1930.



Quain houses. Salttjern 29/1 1929.

The dwellings of the district may be generally referred to as belonging to one of two types: 1) The Lapp cabins, and 2) The Quain houses, being of a kind with the dwellings of Norwegian families here.

The photographs on p. p. 39, 40 and 41 clearly show the difference between the two types.

1) *The Lapp cabins* are invariably of one storey and low.



Quain house. Skallelv 11/1 1930.



Quain house. Golnes 5/1 1930.

Most of them are log-cabins, with only very few mud-huts or dug-outs.

The log-cabins are all of them built on the same lines, and they vary very little as to dimensions.

Through a narrow doorway one enters a narrow passage (»fiaeskir»), used for a depository of household articles; from here a door leads into the dwelling-room (»stoppu»), so low

that an ordinarily tall man has to mind his head on account of the ceiling beams. This room is pretty dark, having only one or two small windows with knee-high sills. Besides the room, we occasionally find a tiny closet. — The floor area is commonly 3 metres by four, and as rule there is a low cock-loft, accessible by means of a ladder. — The whole family, from the nursling to the old people, live here, and all the food is also cooked in this room. The atmosphere of the room is accordingly very stuffy and extremely distinctive —



Quain house. Golnes $\frac{5}{1}$ 1930.

an atmosphere that the Lapps carry along with them, and which does not tend to make them very welcome guests in better houses. The smell is due to their clothes, which they wear day and night — sleeping in them, in fact — and seldom change, and it also emanates from their bodies, that are very seldom brought into contact with water.

Garments of reindeer skins form part of their regular winter equipment, to an extent far and away in excess of what is usual with Norwegians and Quains, and this — as mentioned in a previous section — may be the cause of the Lapp women, and their somewhat elder children, being able to spend more time outdoors than those of the other races.

Each of the Lapp families included in my materials has,

on an average, 1,3 rooms, with an aggregate capacity of 53,2 cubic metres.

2) The Quain houses, too, are of a distinct type. As a rule, the dwelling-house itself contains 1—2 rooms, a kitchen, and a loft. The cow-house invariably forms an addition to the main building, generally on the north side, and is covered by the same roof — whilst the Lapp shelters his animals in a dug-out situated at a short distance from the cabin. In the case of the Quains, as well, the kitchen is the regular living-room of the family. It is generally a fairly large room — for instance, 4,5 metres by 3,5 by 2,3. This kitchen is generally cleaner, with more light and better ventilation, than the Lapp »stoppu».

The peasants of Finland — in which country there is a hot-air bath-room on every farm — probably constitute the cleanliest peasantry in the world. In Finmark, where wood is scarce, the Quains have to make the best of it; but still, there is, at least, one bathing establishment in every hamlet, where the inhabitants regularly take a hot-air bath once a week, or fortnight, and change their underwear.

At Skallelv, each family has, on an average, 2,06 rooms, with an aggregate capacity of 86,4 cubic metres.

The average for Golnes is 2,1 rooms, aggregating 63 cubic metres.

As to dwellings and cleanliness, the Norwegians of the district compare with the Quains, from whom they have caught the hot-air bath habit.

CHAPTER II.

Rickets in Relation to Diet.

After having in previous sections disposed my materials, and tried to establish the effects on rickets of factors — other than diet — pertinent to the Vadsø district, I have now arrived at the second question to be dealt with in this paper.

I shall commence with an account of *The General Diet* in this district, where *fish* constitutes such a dominant part of the ordinary food-stuffs. This diet may well be thought to have an effect on the infant, partly through the parents — at all events, through the mother — and partly in a direct manner, from the time the child begins to partake of the ordinary family meals, a thing that usually happens at an early age in this district.

Next to follow is a statement as to *The Specific Diet for Infants*.

Finally, I shall introduce a discussion on *Rickets in Relation to Diet*, more particular in its relation to a *fish diet*.

The Fisheries. — These are carried on in the Varanger fiord itself, and never so far from land that the fishermen do not return every day with what they have caught. Cod and haddock are caught all the year round, but most, as a rule, in March, April, and May. From Johnsmass to Christmas quantities of coal-fish are taken up. These are the three species essential to the families of the district — other kinds are fished for in order to procure necessary cash.

After 1917 and 1918 — in which years it was thought that the fish were chased out of the fiord by seals — the

fishing has regularly been good, at least, as regards the supply for the population of the district. (This statement takes no count of a reservation made later on regarding the fishing stations east of Vadsoe, during the autumn of 1929).

In a subsequent distinction between fresh fish and liver, on the one hand, and salt fish, with or without oil, on the other, I have especially taken into consideration that liver, and liver oil, are the most important vitamin sources.

Supply of fresh Fish. — At the innermost parts of the fiord the sea is so smooth that fishing may be carried on every day, all the year round. Small boats — *i. e.*: row-boats without motor — are employed, and, practically speaking, every single family has a plentiful supply of fresh fish at all times of the year.

A little further out, near Jacobselv and Vadsoe, the sea is rougher and does not favour regular fishing excursions in small boats during the most boisterous winter months. However, each of the above places has a harbour for big boats — *i. e.*: decked motor vessels — and with such boats the daily supply of fresh fish is ensured at all seasons. This is also the case with Bugoynes, where there is an excellent harbour.

Andersby has no harbour — a circumstance which affects the supply of fresh fish during the worst winter months. This likewise applies to all hamlets east of Vadsoe, and in a higher degree according as the fiord opens out. Not a single harbour for big boats is to be found at these places, and even the estuary of Skallelv is entirely unsuitable during stormy winter months. For these hamlets the fishing becomes extremely difficult during the months from October to January (both included). Whilst there is a plentiful daily supply of fresh fish during eight months of the year, this ordinarily is reduced to a supply twice a week during the four months mentioned above. The supply is even less at Ekkeroy, where the inhabitants have, in a measure, lost their liking for the sea, on account of the relief works started on shore.

Exceptional Conditions prevail at Skallelv. — The largest holdings belong to the inhabitants of this hamlet, who likewise own excellent motor fishing-smacks. Nevertheless, the supply of fresh fish is exceedingly poor all the year round.

During the six months, September—February, weeks may pass when many families — most of them, perhaps — do not see any fresh fish at all: and even during the favourable months, there is a general scarcity of this article. This is owing to the fact that the Skallelv fishermen regularly start out from Varðoe and Vadsoe in their big boats, and carry their catches straight to these ports, without calling at Skallelv. Fresh fish they once in a while send home by local coasting steamer, but — be it understood — invariable in a gutted state, and minus any liver.

In all other cases, when there is a mention of fresh fish as an article of diet, it should be understood to mean a consumption of liver, as well. *Generous quantities of fish liver are invariable consumed along with fresh fish.* Even at times of minimum liver content in fish — as during the dark season — the fishermen have excellent opportunities to pick out the largest and best livers for their own use.

Salt fish. — On days when there is no fresh fish to be had, salt fish is generally eaten instead — and at Nesseby, more of the frozen article. Consequently, the consumption of salt fish is greatest during autumn and winter, more particularly so in hamlets situated east of Vadsoe. Besides being a matter of necessity, a natural craving for variety has to be taken into account. Especially in the case of the Quains, the consumption of salt fish is considerable, even in hamlets where there is a plentiful supply of fresh fish. This may perhaps be a reminiscence from Finland, where salt fresh-water fish is in great favour.

At. V. Jacobselv salt fish is thus served every other day, alternatively with fresh fish, the latter being partaken of on days when the nets are drawn.

Salt fish — or frozen fish — is eaten with fish-oil, lard,

bacon, or margarine. — When speaking of *fish-oil*, I mean the fat which is extracted from fish livers and kept for future consumption with salt fish — in contradistinction to »*moelje*» which is the fat extracted by boiling the livers and intended for immediate use, and which is always served with the fresh fish meal of the day.

Fish-oil. — Formerly, before the days of steam oil-refineries and margarine, fish-oil was used in every household of the district. Even at the present day, this liver is of such importance as an article of food as to call for a special mention here.

The household oil of the district is mostly made from the livers of coalfish, but frequently, also, from cod-liver.

The quantities of liver in the fish, as well as the oil content of livers (the oil percentage), may vary considerably from one season to another, and from one year to another.

For the coalfish caught near Vadsø in 1929 the following variations were found:

On June	19th	940	kilos	of fish	yielded	1	hectolitre	of liver,	with oil per-
									centage = 28;
» July	13th	715	»	»	»	1	»	of liver;	
» August	15th	820	»	»	»	1	»	»	»
» Septbr.	3rd	890	»	»	»	1	»	»	»
» October	2nd	960	»	»	»	1	»	»	with oil per-
									centage = 43.

For codfish caught in the Varanger fiord, the same year, the figures are:

In April	1,700	kilos	of fish	yielded	1	hl.	liver,	oil	percentage	25;
» June	1,800	»	»	»	1	»	»	»	»	35.

In 1926 the liver content was considerably larger, 800 kilos of cod yielding up to 1 hectolitre of liver.

However, these variations may perhaps not be of very great importance as regards the quantity and quality of the home-made oil of the district, for — as we have seen — the fish-

ermen are always able to pick and chose the finest and largest livers.

We have also to consider that the vitamin content of a liver is thought to be inversely proportional to its weight (POULSSON).

The data given above are merely intended to show that I am fully aware of the oil here in question not being of any standard quality, but of a quality that may be said to vary more or less. Matters become considerably worse, however, when the fisheries fail, as was the case in the autumn of 1929, when — after good summer fishing — the coalfish failed to appear, so that the hamlets east of Vadsoe, trying to lay in their winter stores of salt fish and fish oil, had to be content with half the usual quantities of these necessities.

For trying purposes, the finest livers are selected, which — the gallbladders being removed — are washed in several changes of water, and then left to soak throughout the night. With a little water in a large cooking-pot the liver is then set to boil at a slow fire (fast boiling being always avoided), and the fat is skimmed off with a spoon as soon as it appears on the surface. This fat is finally given a quick boil up, after which it is bottled, with a little salt and some whole pepper. I have not been able to gather any information as regards the vitamin content of this oil. Having regard to the stability of vitamin D, we may reasonably suppose that the vitamin value of the home-made oil should not fall very much short of that of medicinal codliver oil.

The old way of preparing oil — sometimes still in use amongst the Lapps — is to fill the liver into large barrels, which are then left alone until the pressure and the action of decomposition liberate the fat contained in the adipose cells. I have mentioned this in order to give some idea as to the degree of fastidiousness and appetite displayed by the Lapps in the case of fish oil — the oil prepared in the manner just described being of very strong smell and taste, and hard to digest.

Besides being a cheap and nourishing fat to serve with

salt fish, fish oil is used by some families for the frying of fish, and in preparing various fish dishes. In the absence of margarine, the Lapps are still occasionally seen dipping their bread in fish oil.

Next will be given an account of the quantities consumed of fresh fish and liver, and of salt fish and fish oil, in various parts of the district.

Quantities consumed. — As regards this question, there is a distinct difference between the Lapps and the rest of the population. Large quantities of fish are consumed in all parts of the district, but the Lapps are well ahead of all others in this respect. I shall commence with giving a few typical examples from some of the Lapp families — the daily allowances of fish are to be reduced by $\frac{1}{3}$ for wastage:

- 1) A family consisting of 3 adults and 1 child of 5 years of age generally consume about 4,5 kilos of fish, *i. e.*: about 1 kilo per individual, and the livers of 4—5 fish.

During the autumn, the same family prepare more than 1 anker (about 39 litres) of fish oil, and salt 1 barrel (about 100 kilos) of split fish.

- 2) A family of 2 adults and 6 children (of which 4 of school age, and 2 younger) consume, on an average, 0,8 kilo per individual per day, besides the liver of 5—6 fish.

In the autumn this family prepare 30—40 litres of oil — which quantity is consumed before Christmas — and 3 barrels of salt fish.

- 3) A family of 4 adults and 5 school children consume, on an average, 0,9 kilo per individual, besides the liver of 4—5 fish.

The Lapps generally eat their fish without potatoes, only with bread. A Lapp told me that a grown-up man would require upwards of 1 kilo of fish, served with liver and bread — if served with potatoes, he would be likely to eat more.

As we have seen, the daily consumption is wellnigh incredibly large — something like 1 kilo per individual — even the children not being, apparently, very far behind in this respect. As is the case with natural man generally, the Lapps have no sense of moderation in food, and their meals are also partaken of in a somewhat primitive manner: — The members of the family are generally seated on low stools around the only two articles of table furniture employed. These articles are, a steaming dish of fish, and a jar of fish oil. They all eat with their fingers, helping themselves from the common dish to pieces of fish, which are then dipped well into the common jar, so as to fetch up as much oil as possible.

«Moelje» and Fish oil are the predominant fats with the Lapps, and these articles are used in every family. Some salt fish is used, as well as frozen fish, particularly during the two darkest months.

In other parts of the district we find greater variations in the weekly consumptions, as a few more well-to-do families in a couple of the hamlets do not have fish every day (a further account of which is given later on). In consequence, the lowest figures, of those given below, may be somewhat too low, as they are computed from the consumption during 1 week. Otherwise, the following figures are typical as regards the Norwegian and Quain part of the population:

- 1) A household of 4 adults consuming on an average 500—600 grammes of fish per individual per day. Daily consumption of fish oil is 70 gr. per individual.
- 2) Two adults. Average daily consumption of fish 3—400 gr. per individual, and consumption of oil 40 gr.
- 3) Four persons of ages 8, 20, 50 and 51 years. Average daily consumption of fish 300 gr. per individual. Consumption of oil 40 gr.
- 4) One family who consume 700 gr. per individual.
- 5) One family who consume 450 gr. per individual (4 adults).

- 6) One family who consume 5—600 gr. per individual (5 personers above 15 years).
- 7) Household of 5 adults and 2 children under 7 years, consuming on an average 5—600 gr. per individual, per day.

The average daily portion per individual works out at about 600 grammes, which is, as we see, considerably less than that of the Lapps.

As has been mentioned before, liver is always partaken of with fresh fish, but the consumption of liver is also somewhat less than in the case of the Lapps. Potatoes are served with the fish for dinner (the mid-day meal). The way of using fish oil is to pour it over the fish, so that the latter is generally »swimming» in oil.

Individual variations exist, of course. Thus, an inhabitant of Hoivik told me that he and his grown-up son, between them, consumed as much as 1 litre of liver with their daily allowances of fish, but this must be considered a somewhat uncommonly large consumption of that article. The figures given above show the consumption of fish oil in a few families. With regard to such consumption, individual variations are apparent in Norwegian and Quain hamlets, to an extent that is far in excess of what is to be observed in the case of the Lapps. Some families use fish oil, others do not; and the same may be said to hold good — in some measure, at least — with regard to the individual hamlets.

This point being of some importance, a few facts are given below by way of illustration:

Skallelv is conspicuous once more, which is due to quite natural causes. The failure as regards a supply of liver in this hamlet, has been mentioned before. Consequently there is nothing to prepare the oil from, and of later years only quite a few families — in the autumn of 1929 only two families — have been able to make any oil at all.

In *Ekkeroy* the consumption is below the average, as many families do not use any oil. Thirty litres per family

was the maximum, as given me last autumn (1929), whilst the ordinary consumption was something like 5—10 litres.

In Krampenes the inhabitants generally use much fish oil. Excepting a couple of families who never use any, the general consumption was stated to be about 20 to 30 litres per family, for the six winter months. A household of 5 adults and 1 eleven-year old girl consume about 100 litres per annum. — Another household of twelve persons, including several infants, last autumn prepared about 60 to 70 litres of oil, which quantity lasted till the end of February — a consumption of about 1 litre per individual per month.

In Golnes fish oil is used regularly. In the autumn of 1929 5—20—30 litres of oil was prepared per family.

In Bugoynes the oil consumption was similar to that of Golnes.

In Kiby the consumption is irregular, as many of the families do not use oil. For the autumn of 1929 the figures were 5, 20, 30, litres per family.

In Vadsoe the consumption is *nil*, there being only four families who use a little fish oil. (In this town the taste is generally too »refined».)

In Jacobselv some oil is consumed, but the two steam refineries here secure the greater part of all the liver.

In Mortensnes the oil consumption is something like that of Nesseby. A couple of families do not use any oil, but the others use much — 30 to 40 litres being an ordinary consumption from autumn to spring. A family of 4 adults and 3 children used 100 litres per annum — so I was told by the head of the family.

As will appear from what has been stated above, many Norwegian and Quain families use a good deal of fish oil, whilst some families use but little, and some none at all. And it has also been shown that the same statement is true with regard to the various hamlets. — The quantity of fish oil consumed by one single individual varies from 0 to 70 grammes a day. This latter figure does not, however, hold good for

every day of the week. An oil consumption of 30 to 40 litres during the six winter months is nothing out of the common for a fairly large family — not taking account of the autumn of 1929 (*vide* page 27) — and this works out at about 1 litre per individual per mensem, or a daily consumption of about 30 grammes. A man from Kiby, who generally took 70 grammes of oil at one meal, told me that oil was not served at all more than three days a week.

In the Lapp families, the individual portions of oil do not differ much from the larger ones mentioned above, *but fish oil is used in every household, and the article is at hand at all times.*

Finally, a statement as to the consumption of *Salt Fish* is given:

The largest quantities are consumed in Quain hamlets, and in the hamlets situated east of Vadsoe, with Skallelv, Ekkeroy, Jacobselv and Krampenes taking the lead. In these hamlets, quantities of about 100 kilos for each adult individual, consumed during the 6 winter months, is nothing out of the ordinary. The largest families (12 persons) salt 7—800 kilos (7—8 barrels). In the other hamlets, including Bugoinen and Kiby, the quantities salted are between 1 and 4 barrels, according to number of household members. In the town of Vadsoe the quantity of fish salted is negligible.

The quantities mentioned above especially apply to the fisher-folk of the district, but — with some small reduction — to other people of the poorer classes, as well.

Even in the comparatively few well-to-do families, fish is generally served for dinner several times during the week.

In most of the homes of the fishermen, fish is served for dinner on the six week-days, frequently on Sundays as well. When there is a scarcity of ready money to buy flour, boiled fish is served twice, or, perhaps, three times a day.

In Skallelv, where there is plenty of milk, and also some meat to be had — and in Vadsoe, where money circulate a little more freely — many of the fishermen have fish only four or five times a week.

Fish is usually boiled for dinner, and liver is either boiled or fried: by the latter treatment, especially, liver yields plenty of oil. As a matter of curiosity, it may be mentioned that the Lapps are very fond of a compound of liver and oatn groats stuffed into fish-guts and boiled.

Hard roe is used to some extent. This article is of interest on account of its vitamin content.

Variously prepared fish dishes are served in more refined households: in Vadsoe this is the case to some considerable extent.

By second-hand information from the National Vitamin Institute I have learnt that vitamin D exists in fresh fish, salt fish, and in variously prepared fish — as well as in liver and liver preparations — but that quantitative conditions have not been determined. I cannot be sure whether the vitamin content in fish flesh may be of practical value, so I have to rest satisfied with taking the large consumption of fish as an indication of a good appetite for liver and fish oil as well.

Before passing on to a brief statement as regards the few other articles of food included in the plain fare of this district, I am going to summarize the information I have been able to gather respecting the consumption of fish in the various hamlets. *Vide* Table VI.

Table VI.

	Consumption of Fish, Liver & »Moelje»	Consumption of Fish-Oil	Supply of Anti- Rachitic Vita- mins
Skallelv	insignificant	insignificant	0
Ekkeroy	small	below average	+
Jacobselv	average	average	++
Golnes	below average	average	++
Andersby	below average	average	++
Vadsoe	average	insignificant	++ ¹
Krampenes	above average	above average	++
Nesseby	large	large	+++
Kiby	average	average	++
Bugoynes	large	average	++
Mortensnes	large	large	+++

¹ By way of contrast with Ekkeroy, I have noted Vadsoe with ++, as fresh fish and liver are used in all families, there, whilst fish oil is used in very few households of Ekkeroy.

The supplies of vitamin D (third column) are characterised by 0 for minimal, + for small, ++ for moderately good, and +++ for plentiful, giving totals based on the two other columns. It should be safe to take the totals in this way, as the other articles of food — not yet mentioned — must be assumed to carry negligible quantities only of the particular vitamin in question.

I shall be referring to Table VI in the course of the discussion on influence of diet on rickets.

Milk. Most fishermen living in this district keep 1 or 2 cows, and in places like Ekkeroy — especially *Skallelv* — a larger number. In the latter hamlet there are 100 milch cows for the 223 inhabitants, who sell but little of the milk and no butter. At such a place, milk is of very great importance, and the inhabitants live largely on porridge, and take milk instead of coffee.

Bugoynes is one of the hamlets where milk is most scarce, as there are only 20 cows for the 400 inhabitants. Nevertheless, and in spite of the fact that most of the cows were dry on my visit there in January 1930, the children examined were all excellently well-nourished.

The cows of this district usually calve after Christmas, and consequently they are dry during the darkest months of the year. During the spring there is generally little milk, on account of a scarcity of fodder. In the months of June (partly), July, August, and, maybe, September, the cows feed in the grazing-grounds, and probably give very good milk. No examinations, with a view to ascertain the percentage of fat in the milk — far less as to its vitamin content — have ever been made in this district. In the course of winter and spring the milk probably deteriorates considerably. At many places, and especially with the Lapps, all the hay is stored outdoors, which probably is not the best way of doing it.

Wherever there is little milk to be had, coffee is taken

instead, and children are frequently given coffee from they are two years old.

Natural butter is hardly ever used.

Bread is practically always baked from mixed wholemeal, and mostly home-made. The daily allowances average 700 grammes per individual. When milk is taken with the bread, margarine is frequently dispensed with.

Porridge is extensively served for supper, and for dinner some grit or water gruel, after the fish. Porridge is most frequently made from rice, mannacroup, or semoule — very seldom from oats.

Potatoes are mostly used by Norwegians and Quains, who grow them to some extent, themselves. The Lapps may buy some potatoes during the autumn, when they are cheapest, but they mostly go without.

Meat is a rare article, and is almost exclusively reserved for the Sunday dinner.

In the autumn, cloudbberries, blackberries and cranberries form an important part of the diet.

The state of nutrition. In order to convey a general idea as to how far the articles of food enumerated above are likely to constitute a sufficiently comprehensive diet, according to modern standards, I have tabulated the average daily quantities partaken of by a grown man, Table VII, page 59. (This table is worked out according to *Nahrungsmitteltabelle*, by SCHALL HEISLER.)

The most important divergencies from the diet scheduled in Table VII are given below:

- 1) In some parts of the district — more especially during the winter months — practically no milk can be included in the diet, which causes a most serious reduction — down to about 0,5 grammes — of the daily supply of CaO. For the more milk-abounding parts of the district we may assume a

higher figure than the 500 grammes given in the table — which signifies a satisfactory supply of CaO as of vitamin A (growth-promoting).

2) The quantities consumed of liver and fish oil are also highly varying, which is of interest as regards the supply of the fat-soluble vitamin, and especially of the antirachitic vitamin (*vide* Table VI, p. 55). The variation also effect the calorific value of the diet. During the cold season, involving the greatest expenditure of energi, a stronger craving for liver and fish oil is involved as well. In parts of the district where these articles are more scarce, the requisite calories are supplied by a correspondingly increased consumption of milk and milk-food (porridge).

3) The figure denoting the supply of NaCl is at a very low estimate, and it would be considerably higher for the hamlets where most salt fish is consumed, as the fish is invariably eaten in a very salt condition. With the reservations already mentioned as regards vitamin D and the supply of lime, the general diet of this district must be considered good, and as fully satisfactory with regard to the various requirements. The liberal supply of proteins is a characteristic feature of this diet, as is also, in a measure, the abundance of fat and of the fat-soluble vitamin, which may be far in excess of the quantities indicated by the figures given in the table. The supply of NaCl should also be noted, and the scarcity of CaO — a scarcity which is real in itself as well as compared to the supply of P_2O_5 . As for the women, the allowance of fish — and, consequently, the supply of P_2O_5 — may be somewhat smaller than given in the table, but this does not affect the supply of milk, nor, consequently, that of CaO, which remain as tabulated.

The general quality of the diet impresses me favourably, also when judging from the state of nutrition of this population. The men are robust, muscular, and in fit condition. The women, who have much indoor work — which is partly of a heavy nature — do not look so well, whilst the children have, generally speaking, a very fit and healthy appearance.

Judging from Dr. SCHIØTZ's table of children of »Marked Underweight», my materials from 1928 and 1929, of school children, show that 11,8 per cent. were of »Marked Underweight». This is an excellent result, as compared to similar examinations made in other parts of the country, where the following percentages were found:

At Dale (Western Norway) 28,6 per cent.¹

» Glommen (Eastern ») 12 to 19 per cent.

» Opdal (the Trondhjem part) 11,2 » »

» Ulstein (Søndmør) 22 » »

» Tromsøe 12,4 » »

Table VII.

	Daily Allowance, in gm.	Proteins	Fat	Hydrates of Carbon	Calories
Fresh Fish	700	109	2,1	0	539
Fish Liver	100	6,7	4,8	7,6	103
or					
Fish Oil	50	0	48,5	0	460
Bread	700	32,9	4,2	335	1.540
Milk	500	16	18	24	335
Margarine	70	3,5	59,2	2,8	553
Sugar	70	0	0	68,5	274
Wheat Flour (porridge)	100	8,7	0,9	71,2	335
Potatoes	200	3	0,2	40	176
With Liver:		179,8	89,4	549,1	3.855
With Fish Oil:		179,1	133,1	541,5	4.212

In the above diet, the contents of anorganic substances, are:

upwards of 6,0 gm NaCl

about 5,4 » K₂O

» 1,5 » CaO

» 6,0 » P₂O₅

There is a good supply of accessory alimentary substances, especially a plentiful supply of the fat-soluble vitamin.

¹ Tidsskrift for Den norske lægeforening, no 5 and 9 1929 (Periodical for the Association of Norwegian Physicians).

The Nourishment of Babies.

Before passing on to a discussion on the relation of ordinary diet to rickets, I am going to treat of the special diet of babies, the relation of this diet to rickets, and of the infants' changing over to the ordinary family meals. It will perhaps be difficult to determine — with the clinical facilities ordinarily available — whether the influences of a fish diet, affecting any child through its mother, may be of a prenatal or a postnatal nature (through the mother's milk or otherwise).

Experiments with animals and human beings seem to prove that the vitamin D content of milk is inconsiderable, and can be but slightly varied by supplying the mother with fish oil. The prenatal supply of the vitamin may possibly have greater effect.

It should therefore be understood that, when — in a subsequent section — discussing the relation of an ordinary diet to rickets, I am always keeping in mind an indirect influence through the mother, as well as the direct one, even though both effects may be spoken of collectively.

As to the diet of the pregnant woman, or the nursing mother, there is nothing to be said beyond what has already been mentioned in the section on general diet, with this addition, only, that her greater need of CaO cannot be easily satisfied, considering the strictly limited available supply of this substance, as shown in the table. The tenor of her daily life does not deviate from the usual lines, except for about a week in childbed. The heaviest work rests on the women of the district. Besides being in charge of the house and the numerous children, she has to attend to the cowshed and give a hand with in connection with the day's catch of fish. During summer and autumn she has to take a part in grass-cutting operations and in peat-working. Their daily working-programmes are filled out in such a manner as not to leave the women much time, nor strength, to devote to their little ones. As, moreover, in great parts of the district,

the knowledge of child hygiene — and of general hygienics, — is at a very low level, it is hardly surprising that the infant deathrate figures are as high as is actually the case. In the course of the last decennium the deathrate figures for less than one year old infants show upwards of 100 deaths per 1000 quick-born babies. For the rural district the figure approaches 120, and for the town of Vadsoe it is about 105.

Nevertheless, on the whole, the nutritional condition of infants is good. The children are, as a rule, big, vigorous, and somewhat over-fed. In my description of them the term »somewhat too plump» has been frequently employed. Atrophic children are rarely seen. In order to acquire a better idea as regards the influence of a fish diet on children, I examined, on January 13th and 14th 1930, in the industrial town of Kirkenes in South Varanger, 71 children of ages from a couple of months up to 5 years. In respect of these examinations I made the mark that there were many small, underweight children (of tender years as well as older) the nutritional condition and growth of whom were below standard. Rachitic deformities of the osseous system were observed in 34 children out of the 71 examined. I cannot help thinking that several more of these children would have carried signs of rickets, if they had been less slow of bodily development.

In Kirkenes, fish liver and oil constitute but an insignificant part of the general diet. Milk is hard to procure, and not always of the best quality, owing to the transport from Tromsøe. Condensed milk is used to a considerable extent, also much flour, in the food for infants. A deficient supply of the fat-soluble vitamin might thus be reasonably expected, and this seems to agree quite well with my impression of the children.

During the autumn of 1929 — having commenced to doubt the correctness, in many of the cases, of information received as to the diet of infants — I had an inquiry form printed and distributed. By kind assistance of schoolmasters, midwives, parish sisters, and parents, I succeeded in getting

the forms filled in for, practically, all the 376 children. By comparing these forms with my previous notes, and then re-questioning the parents in all cases of discrepancy, I hope to have acquired sufficiently copious and reliable information as to the diet of babies.

Out of the 376 children below school age, 203 were breast-fed, 138 of varied nourishment and 35 artificially nourished (bottle-fed).

As *breast-fed* babies I have considered those who received breast, exclusively, during the first 4 months of existence.

As children of varied *nourishment* I have counted those who were breast-fed and given other nourishment as well, in between, within the first 4 months.

As *artificially nourished* I have characterized the children who have never, practically speaking, received any breast at all. All the 35 belonging to this category have been fed with diluted cow's milk, from a bottle.

Breast-fed. Out of the 203 breast-fed children, 65 are rachitic, that is to say 32 per cent.

In the Faroe Islands, Dr. A. RASMUSSEN found 34 per cent of breast-fed children to be rachitic. This percentage, however, only applies to children of less than two years of age, and who had been examined several times within this first period of their lives.

Only a small minority of the breast-fed children have been fed according to anything like a rationally ordered plan, with regular meals. The information that *the child was fed whenever it cried* recurred with such frequency that I had to make especial mention of it in my inquiry form. In general, the children have been given the breast too frequently — have been overfed, in fact. Out of the total number of breast-fed children, 77 were given the breast for a longer period than 12 months; 18 months was not uncommon, while instances of children receiving suck during 2—3 years are not wanting, though of very rare occurrence. Of these 77 children,

35 per cent. were rachitic. That the percentage is not higher, may possibly be due to the children of this district being given other food in between, at an early age.

Varied nourishment. Out of the 138 children of varied nourishment, 78 are rachitic, that is to say 56,5 per cent. Most of the overfed children belong to this group.

In my materials, a varied nourishment signifies — in the great majority of cases — the breast, and, when the child has attained an age of a month or two, diluted cow's milk from a bottle. An account of this mixture will be found in the section next below. It is more especially the Quains who favour this form of nourishment. (*Vide* Table VIII.)

Artificially nourished. The 35 belonging to this category are all of them bottle-fed children, 19 of whom — or 54,3 per cent. — are rachitic. My impression of these children is that they are not liable to over-feeding, to the same extent as are those belonging to the previous group. As a rule, the bottle-milk is not boiled; it is diluted with boiled water or with broth, or it is given undiluted. The mixing is done at random, and I was often told that they gave the children pure and diluted milk, alternately. The quantity frequently exceeds 1 litre a day. Regular meal hours are very rarely fixed, and a child is often allowed to suck at its bottle during considerable parts of the day.

No great error would accrue by regarding the two last groups as one. We then get a total of 173 children, of which the 97, or 56,1 per cent. are rachitic.

In table VIII, page 65, the 376 children below school age have been disposed according to the distribution of rickets within these groups, for each separate hamlet. In column 4 will be found the percentages of »not breast-fed» children (groups 2 & 3 added together). The hamlets have been ranged in sequence of the percentages of rickets.

Excepting for Andersby and Krampenes — which hamlets have the smallest number of examined children, and where,

consequently, sources of error would have the fuller play — we perceive that column 3 shows, broadly speaking, a fairly gradual decrease in the percentages of »not breast-fed», from the 65,9 per cent. of Skallelv down to the 5,9 per cent. for Mortensnes. Deviations from the regular drop in the percentages are, however, presented by Golnes and Nesseby, the deviation in the latter case being of the more pronounced nature.

In the section on »Out-of-door life» the connection between »little out-of-door» and »little breast» has been discussed. In a subsequent section these two factors, and their relations to rickets, will be illustrated by a curve (Curve II).

Transition to ordinary diet. At quite an early age the infants of this district begin to partake of other food, besides mother's milk or cow's milk. They commence, as a rule, with a tea-spoon full of thoroughly mashed fish moistened with »moelje», a little porridge (of manna-semolina), and milk from a cup. This diet is frequently commenced with at an age of about four months. In the course of the next following weeks the quantities of fish and »moelje» are gradually increased, and some liver is generally added. Later on the child is given some bread, and, when about a year old, some salt fish and fish oil — from now on, it is partaking of, practically, everything which constitutes the ordinary diet of the adults. In the cases of 334 children I have made note of the ages at which they commenced to have their share of the ordinary family diet (especially of fish). It proves that the rachitic children included in the above total commenced to partake at an average age of 8 months, whilst the average age for the non-rachitic ones works out at $6\frac{1}{2}$ months. That both these averages are pretty high, must undoubtedly be due to their being strongly affected by the comparatively few children who commenced to partake at a very late period, and also to the fact that the early age of 4 months mentioned above, more especially applies to the rural population, whilst the children of the town of Vadsoe generally commence to partake at a somewhat later age.

The ages at which children commence to partake of ordinary fare seem to bear some relation to rickets, to the effect that children who begin to partake at a comparatively early age might, perhaps, be less liable to get the disorder than those who do not.

Table VIII.

	Number of breast-fed, having		Number of varied nourishment children, having		Number of bottle-fed having		Percentages of not breast-fed
	R—	R+	R—	R+	R—	R+	
Skallelv	6	8	4	17	1	5	65,9
Ekkeroy	3	2	2	5	0	1	61,5
V. Jacobselv	4	6	4	3	2	3	54,5
Golnes	8	4	9	12	1	0	64,7
Andersby	4	1	0	1	1	0	(28,6)
Vadsoe	56	26	16	23	4	4	36,5
Krampenes	6	2	1	1	0	1	(27,8)
Nesseby	13	8	19	11	2	0	60,4
Kihy	8	2	3	2	0	1	37,5
Bugoynes	17	3	2	3	4	4	39,4
Mortensnes	13	3	0	0	1	0	5,9
	138	65	60	78	16	19	
	203		138		35		

This finishes my account of the diet, and I am next passing on to a discussion as to its relation to rickets. As previously mentioned, a direkt influence on the child through its mother may have to be considered, as well as an indirect one. Neither of these considerations would be neglected, if the differences in the diet of the various hamlets — commented on in a previous section — be made the basis of the discussion.

A Discussion on the Relation of Diet to Rickets.

With the exception of diet, the relation to rickets of the various factors to be considered in the Vadsoe district, have been discussed in the previous sections.

(Cases of premature birth, and of twins, have been entered in the record sheets, but they have not been collectively discussed in the present paper, as these two — in themselves very important — factors are of such rare occurrence as to be of, practically, no effect in my materials).

As regards the influence of the »town»-wise appearance of rickets in this district, I shall, for the sake of lucidness, divide the rickets-producing factors in »dominant» and »non-dominant» factors.

What I have found regarding these factors, may be summed up as follows:

»Non-dominant» factors. In my materials, considered in the aggregate, age and sex of examined individuals are factors of importance. When, however, a comparison is involved as to the frequency of rickets in the 11 (13) hamlets, the above factors do not cause any disturbing effects (*vide* the respective sections).

Conditions of habitation and of general sanitation have no assignable effects, even in the aggregate materials, and, consequently, they can not influence the »town-wise» appearance of rickets.

Race. In previous sections I have been unable to fix the importance of this factor with any degree of certainty. It will, however, be referred to in subsequent pages.

Climate. In a general way, the climatic conditions are alike in all parts of the district. This subject is also referred to further on.

»Dominant» factors. These include the factors that are not only highly effective in themselves, but which also vary appreciably from one hamlet to another, and so become distinctive features of the »town-wise» distribution of rickets.

I have previously made mention of two such factors, *viz.*: »Out-of-door life» and »Bottle-feeding».

In the present section I am trying to determine the effects of *diet*, and I think that the differences in nutrition in the various hamlets — which differences have been especially pointed out previously — will be found to afford a good and reliable basis for a discussion.

When speaking of the diet factor, I am especially thinking of the vitamin factor, as being its most important component part. However, I am never losing sight of the fact that the inorganic constituents are not to be disregarded, when the question of estimating the relation of diet to rickets is involved. As mentioned before, I am well aware of the scarcity of CaO — in the absolute sense, as well as relatively to the supply of P_2O_5 — as also of the, in some cases, very large supply of NaCl .

The thing that struck me most, from the time I commenced the collecting of materials — and which has also later on caused some reflection — is the exceptional case of Skallelv with regard to the frequency of rickets.

On pp. 16—17 I have endeavoured to convey some idea as to the above mentioned peculiarity (unfortunately, my photographic materials are rather scanty). Curve I, and Table I, also serve to illustrate the same thing. A better comprehension of the matter might be acquired by studying the several record sheets, and comparing them to the couple of photographs given on p. 17. This would be likely to impart a fairly vivid conception as to the extraordinary frequency of rickets in the hamlet, and as to the peculiar character of the disorder as well. Of Skallelv it may be said, that any observed case of a child carrying no distinct signs of the disorder would be quite likely to make one wonder at the reason why.

In looking for an explanation of the excessive frequency of rickets at Skallelv, I shall — before passing on to an account of the »dominant» factors in this hamlet — commence

with a reference to the »non-dominant» ones, in order to find out whether any combination of several such factors might possibly give us something to go upon.

The conditions of habitation are the best in this district, and the state of cleanliness is fairly satisfactory. Economical conditions are not so bad, so that the children are generally supplied with good clothing and may lead a fairly unrestricted out-door life.

The climate is the same as in the other hamlets, at least as in those neighbouring ones with which Skallelv is to be compared further on.

Similar remarks apply as regards *race*, as well.

It is highly improbable that *heredity* should have such an excessive influence in this hamlet; to this factor may hardly be ascribed other than a subordinate, predisposing effect. The fact that the greater part of a family of children generally become afflicted with the disorder — which is the case in most of the families of Skallelv — seems to imply that other factors, which have not yet been mentioned, are in activity.

Age can not be of any essential importance, which is proved by the fact that the percentage of rickets among Skallelv children, of ages from 2 to 7 years, is higher (68,9 per cent.) than for the children of any of the other hamlets, even if the one-year-olds and two-year-olds of these hamlets are included in the count. There are, moreover, severe forms of the disorder, distinctive in the case of the older children of Skallelv.

The *sex factor* has been commented on at pp. 28 and 29.

The two »dominant» factors, »bottle-feeding» and »out-of-door life», play an important part at Skallelv. Nevertheless, the percentage of rickets for the 173 »not breast-fed» children of the aggregate materials is 56, whilst the percentage at Skallelv — though $\frac{1}{3}$ of the children there have been breast-fed — is 73,2.

And again, if we consider the 51 children in Table III (p. 17), we see that the percentage of rickets is about 13 per

cent. lower than that of Skallelv — although *not one* of the 51 children had been taken out-doors during the first year, and in spite of the fact that the percentages for »not breast-fed» children are, practically, the same in both groups (63,5 and 65,5 per cent., respectively).

Of Skallelv's 14 breast-fed children, 8 — or 57,1 per cent. — are rachitic, as against 32 per cent. of breast-fed children in the aggregate materials, and as against 17 per cent. at Mortensnes (where only one of the 17 children was not breast-fed).

Then let us more closely examine Curve II (p. 82), which is drawn from the data set out in Tables I and VII, and is an attempt to illustrate graphically the relations of the two abovementioned »dominant» factors to rickets.

The hamlets that may compare in respect of »out-of-door life» are connected by red lines, the distances of which from the base line indicate the various degrees of »little out-of-door».

For the sake of lucidness I have omitted Andersby and Krampenes, as the very small number of examinations made in these hamlets would be likely to introduce sources of error of inordinate effect.

The curves show that Skallelv and Golnes may compare with regard to the two »dominant» factors. As, moreover, we know that climate and race are identical in the two hamlets, and that other, »non-dominant», factors are not to be reckoned with, it follows that the difference of 26 in the percentages of rickets has to be ascribed to certain factors active in Skallelv, which are not yet determined.

From the curves we get several items of information, which all seem to imply that Skallelv is in quite a peculiar case as regards the frequency of rickets.

In modern researches, Light and Diet are considered factors of about equal importance. They are both of them »dominant» in their relation to rickets.

I have tried to make due allowance for variations in the light factor within the district, principally in discussing the »out-of-door» factor, and also, to some extent, in the section on »climate» (season).

The relation of diet to rickets is a question not yet touched upon, but, having marshalled my facts, I think that this second question may now be made the subject of discussion.

Having due regard to the detailed information given, as to the general diet of the district, we shall now refer to Table VI (p. 32). From column 3 of this table it appears that there is a negligible supply of the anti-rachitic vitamin in Skallelv. Most probably the children of this hamlet will suffer — during pregnancy, and later on during lactation — from a want of this vitamin. At all events, this want is sure to be felt at a later period, when the child changes over to the ordinary family diet. As we have seen, fresh fish, fish oil, and liver, are rarities in this hamlet. Moreover, the above-mentioned changing over to a fish diet takes place at a later period here, where this same diet is chiefly represented by the heavily digestible salt fish.

Considering the great importance of vitamin D in modern researches into rickets, the prevailing conditions at Skallelv strongly indicate *that the extraordinary frequency of rickets at Skallelv is due to a deficient supply of the said vitamin.*

Other diet factors which have to be considered on account of their rickets-producing, or rickets-preventing effects, will be accounted for briefly, in so far as Skallelv is concerned — a reference to NaCl being, however, put off till a little further on.

The large consumption of milk in this hamlet (mentioned on p. 33), combined with the comparatively small quantities of fish consumed, may be expected to afford the Skallelv mothers and children an absolutely, as well as relatively (to P_2O_5), more satisfactory supply of CaO than what is the case in other hamlets — Ekkeroy perhaps excepted. Thus we are bound to presume that, while the large consumption of milk may, on the one hand, serve to retard the development of the disorder, the excessive supply of the growth-promoting vitamin involved may, on the other hand, have an effect in the opposite direction.

(As for Kirkenes, the probable deficiency in both of the fat-soluable vitamins obtaining there has been mentioned previ-

ously. I imagine that this deficiency may, in part, serve to explain the comparatively large number of children of sub-normal growth included in the present materials, as well as the fact that the frequency of rickets, as derived from those same materials, is less than expected.)

We are thus bound to admit that the excessive supply of vitamin A in the diet of Skallelv — together with a deficiency in the supply of vitamin D — must have a certain effect on prevailing conditions in that hamlet.

In order to find out whether similar conditions of diet might prevail in the hamlets lying next outside (east of) Skallelv, I journeyed to Komagvaer (which is the hamlet next to Skallelv, belonging to the Vardø medical district) on September 28th 1929. This hamlet is inhabited by but few Quain families, so that I was able to examine only 12 children. In this hamlet the supply of vitamin D must presumably be similar to that of the hamlets marked ++ in Table VI, as the inhabitants carry on their fishing pretty assiduously (excepting during the four severest winter months), and also partake of some fish oil. — Out-door life of children is as at Skallelv.

If it be at all permissible to draw any conclusions from the random sampling at Komagvaer, we see that the percentage of rickets found — 25 per cent. — does not, at least, tend to disprove the dominating importance of the vitamin factor. *The conditions and position of this hamlet seem to fit quite well into the chain of evidence afforded by the hamlets of the Vadsøe district, tending to prove the dominant importance of the vitamin factor in its relation to rickets.*

The strongest proof of the important relation of the vitamin factor to rickets being afforded by Skallelv, I wish to emphasize — before passing on to a discussion of conditions at other hamlets — *that I consider the peculiar conditions prevailing at this hamlet, in respect of an excessive frequency of rickets, as being principally due to the existing deficiency in the supply of vitamin D.*

In the case of the other hamlets, the proof is not quite as plain as that furnished by Skallelv, and I am anxious that

any uncertainty on this point should tend to shake the evidence afforded by that hamlet. Such uncertainty may arise from the necessity of having to take other factors into consideration, and also, partly, from the fact that the disorder, in the case of the other hamlets, is not of such distinctive character, but generally takes a more normal course.

Nesseby is the hamlet which — next to Skallelv — interested me most, whilst collecting materials, as well as afterwards:

My first and immediate impression of rickets in connection with the Lapps of the district, was that the disorder had not by far such chances of development in their case as in that of the Quains, and this impression was later on confirmed as shown by the figures given in the section on race. Curve II shows that Nesseby — which hamlet, as far as the ›dominant‹ factors are concerned, compares with Ekkeroy and V. Jacobselv — has a percentage of rickets which is only about half of that of the former hamlet, and 25,7 per cent. lower than that of the latter.

Nesseby represents a case opposite to that of Skallelv, being a hamlet where there must exist certain protective forces tending to counteract the two ›dominant‹ rachitic factors.

Now, returning to Table VI (p. 55), we see that Nesseby (Mortensnes) is the hamlet (are the hamlets) of this district having the best supply of the anti-rachitic vitamin.

Ekkeroy, on the other hand, comes next to Skallelv as regards the supply of this vitamin.

I have previously, in the section on race, discussed the influence of this factor on rickets in the case of the Lapps, without, however, being able, at that period, to make up my mind as to the issue. In the section on climate, I have mentioned some minor differences as to climatic conditions prevailing in circumferential parts of the district. In the section on habitation, I have pointed out a certain superiority as regards the winter clothing of the Lapps, as compared to that of the remaining part of the population. Even though I con-

sider this circumstance, as well, as being of but small account, it has to be considered, as possibly affording Lapp women, and their somewhat elder children, a better chance to get out of doors, than what is case with the two other races.

We thus see that there are 4 factors, including the vitamin factor, which have all to be duly considered when attempting to offer an explanation of the relatively — to the two dominant factors — low frequency of rickets at Nesseby (as also in other Lapp families of the district). In order to ascertain the mutual relations between these 4 factors, we shall consider the conditions prevailing at the hamlet situated nearest to Nesseby:

In Mortensnes the *race* is no longer Lapp, nor do the inhabitants wear the typical Lapp clothing, but the *climate* and the supply of *vitamin D* are the same as at Nesseby

Mortensnes is the hamlet with the lowest percentage of rickets in this district, the percentage being 28,2 lower than that of Nesseby, and a little more than half of that of the total number of breast-fed children included in my materials (32 per cent.). Even if we consider that as many as 16, out of the 17 Mortensnes children examined, were breast-fed, still the percentage of rickets must be regarded as markedly low. This fact, seen in connection with the plentiful supply of vitamin at Mortensnes, *tends to lessen in a high degree any probability of Race being a dominant factor*. This places the importance of the vitamin factor on a correspondingly firmer basis.

Finally, with regard to the influence of climate, the facts mentioned below are in disfavour of a supposition that climatic differences within the district — which differences, by the way, I do not admit — might affect the frequency of rickets:

1. The short distances between Skallelv and neighbouring hamlets entirely preclude all differences of climate, but Skallelv represents, nevertheless, a peculiar case as regards the frequency of rickets.

2. Komagvaer, though situated still closer to the »sea

stations», has a decidedly lower frequency of rickets than has Skallelv.

3. Considering the short distance between Mortensnes and V. Jacobselv, any difference as to climate becomes inconceivable. An this is also true in the case of Nesseby—V. Jacobselv. Nevertheless, V. Jacobselv has a distinctly higher frequency of rickets than either of the two other hamlets. It has been previously mentioned that Nesseby and V. Jacobselv may fairly compare in respect of the two dominant factors.

A circumstance which may make comparisons with Jacobselv somewhat doubtful will be referred to further on, when discussing the importance of NaCl to rickets.

4. With regard to »out-of-door» life, Bugoynes may be placed between Golnes and V. Jacobselv. The hamlet lies right in the opening of the fiord, and — if climatic differences are to be considered at all — has a climate similar to that of the most eastern hamlets of the district. But, still, the percentage of rickets is very low here, seeing that only 3 out of the 20 breast-fed children of this hamlet (or 15 per cent.) proved to be rachitic.

In the section on Climate I have made mention of slight differences as to climatic conditions in the circumferential parts of the district. As far as I can see, the facts enumerated above sufficiently prove the correctness of my supposition, that differences of climate, within the limits of the district, are without any importance to the present issue.

At Nesseby — where conditions are the more characteristic on account of the two dominant factors — as well as at Mortensnes and Bugoynes, the abundant supply of vitamin affords a plausible explanation of the inconsiderable frequency of rickets. In a manner of speaking, *these conditions serve to complete the proof as to the importance of diet in its relation to rickets — with Skallelv forming the dark side of the picture.*

As regards the diet factor, the conditions prevailing at Ekkeroy are similar to those of Skallelv, though less characteristic. At Ekkeroy the percentage of rickets, in the case of children below school age, is very high, relatively to the two

dominant factors. The fact that there is a deficient supply of vitamin in this hamlet, seems to agree quite well with what has been previously stated in the case of Skallelv.

Attention has, however, in a previous section, been called to a certain circumstance in the case of this hamlet of Ekkeroy, which tends to create some doubt as to whether the 61,5 per cent. tabulated may not give a somewhat exaggerated illustration of the frequency of rickets at the place. I am referring to the low percentage of rachitism among the school children of this hamlet, and also to the fact that not a single case was entered as being of a severe nature. The matter is so peculiar that one can hardly rest satisfied with regarding it as altogether a matter of chance. Having found no safe explanation, myself, I must be content with calling attention to the following:

Of late years the inhabitants of Ekkeroy have not carried on their fishing with much energy, preferring during the winter months to take part in the relief-work started in this hamlet (the construction of a breakwater). This brought them ready money, but had an adverse effect as to the supply of fresh fish to the hamlet. It was, however, difficult to obtain absolutely reliable information on this matter, and at last I did not know whom to believe — whether the highly envious inhabitants of neighbouring hamlets, or the, on this subject at least, very reticent natives of Ekkeroy. It is not altogether unlikely that the more liberal supply of vitamin, still obtaining a few years ago, may serve to explain the low percentage of rickets in the case of the school children of this hamlet.

As, finally, regards the importance of a liberal supply of NaCl — to which Dr. Hess ascribes a certain relation to rickets, founded on clinical observations — my own notes as to the preponderance of rickets in the Quain hamlets, and in those situated east of Vadsoe, agree quite well with Dr. Hess's observations. In localities where there is a reduced supply of fresh fish — as in hamlets situated east of Vadsoe — and in the case of the Quains, the consumption of salt fish is considerable. This fish is intensely salted, and is consumed

in large quantities. As mentioned on p. 28, a daily consumption of 0,5 kg. per individual during the 6 winter months, is nothing out of the ordinary for a grown-up man. The children get a little salt fish before they are a year old.

The comparatively high percentage of rickets at Jacobselv — in spite of the fairly liberal supply of vitamin D, and of the »dominant» factors which may compare with those of Ekkeroy (*vide* Curve II) — is fairly consistent with an unfavourable effect of NaCl, of which substance there is an abundant supply in this hamlet.

Conclusion.

1. The connection pointed out, between a frequency of rickets and a deficient supply of vitamin, on one hand — and between a lower frequency of rickets and an abundant supply of vitamin, on the other hand — has been repeated so frequently, and is partly so much in evidence, that I consider it *a proof of the anti-rachitic value of a fish diet, more especially as regards the vitamin D supplying components*. As to how far there may be a vitamin D supply of any consequence from any other component parts of the fish than liver, »moelje», fish oil, and hard roe, is a question on which *I am quite unable to give any opinion*.

2. The considerable excess supply of P_2O_5 in the fish diet does not appear to have any promoting influence on rickets, even in cases where the supply of CaO has to be considered as being absolutely low.

3. In my opinion, it is just possible that a large consumption of salt fish may be productive of rickets.

Concluding Remarks.

1. The terms employed in previous sections in order to describe the supplies of vitamin in the various parts of the district, must be, to some extent, understood in a relative sense. For instance, when the supply at Golnes has been characterized as »average», this term is meant to signify that

the supply in question lies between that of Skallelv (Ekkeroy), on the one hand, and hamlets of the Nesseby class, on the other. Thus a supply equal to the above »average» for Golnes would, in the case of most regions of southern Norway, represent one of such magnitude as not to be procurable through the diet alone, but would, probably, compare better with a liberal medicinal administration of vitamin D to mother and child (through cod-liver oil, or special preparations).

The above relativity as to the supply of vitamin induces me to touch in a general way, upon the geographical distribution of rickets, and the influence of the two factors *light* and *diet*. This will be a brief summary only, with no pretensions to anything like a full account (it may be mentioned, incidentally, that literature was hard to come by during most of my stay in the district). Finally I shall append an account of what I have found stated by some authorities as regards rickets in arctic regions.

Of later years, since the researches into *light* and *vitamins* were given a common foundation — as far as the etiology of rickets is concerned — through the isolation, chemically, of the active principle in fish oil, and the activation of ergosterol by ultra-violet irradiation, those two branches of research are no longer in the same sharp antagonism as formerly.

Various parts of the globe are being especially mapped out so as to show the distribution of rickets. Apparently the factor of light is the dominating factor in the case of most regions. We only need to consider the slight frequency of the disorder in sunny tropical regions, as contrasted with its great frequency in the temperate zones, more especially in the least sunny regions, such as, for instance, London and Glasgow — the two cities of Great Britain deriving the least benefit from solar rays. Conditions at Venice, as contrasted to those prevailing in Rome, as also the purdah custom of India, are at present all but classical proofs of the importance of the light factor in its relation to rickets.

Then, into this hegemony of light, the diet factor intervenes. In some of the regions of Japan where rickets and

osteomalacia largely prevail, these disorders are attributed to the diet. The rampancy of rickets during World War and early post-war periods, in the case of the Central Powers, presents a no less striking example to the same effect.

From of old it has been asserted that rickets is of rare occurrence in polar regions and in some tracts of the temperate zone, such as Iceland and the Faroe Islands. This myth is now rapidly falling to pieces. For the Faroes we have the scientifically prepared materials of Dr. A. RASMUSSEN, showing a no inconsiderable percentage of the disorder. For Greenland we have the observations of A. BERTELSEN, and for Finmark the observations of A. WESSEL, which were publicly reported on by Professor YLPPØ at the Third Northern Pediatric Congress, and which fully confirm the presence of rickets in these regions. The Professor held that the fallacy of the old dogma — as to rickets being something entirely unknown or, at least, of extremely rare occurrence, in polar regions — must now be considered as satisfactorily proved. In the course of the same lecture, he further pointed out that the amount of protection afforded by an abundant vitamin content in polar region diet can not at present be accurately estimated.

In Professor GYÖRGY's work: »Die Behandlung und Verhütung der Rachitis und Tetanie», (1929) we find on page 96 the following statements »— — die Seltenheit der Rachitis bei der arktischen Bevölkerung verlangten gebieterisch die Berücksichtigung rein alimentärer Einflüsse» — which statement is evidently founded on the old myth relating to the rarity of rickets in polar regions.

Neither does Dr. HESS give much information as to these regions, in his book: »Rickets, Osteomalacia and Tetany», published in 1929. In the Medical Report of Norway (»Norsk Medicinalberetning») for 1869, Dr. H. K. HARTMANN, district medical officer, reports that rickets is more prevalent in the Vadsoe district than in southern parts of Norway.

According to the above information, we may briefly conclude: 1) That rickets does occur in arctic regions, and that the disorder is far from being a rarity in some parts. — 2)

Owing to incomplete information on the subject, we are as yet unable to arrive at any correct estimate as to exactly how far the generally accepted supposition — as regards the great protective value of a diet rich in fat-soluble vitamin — may be said to hold good.

My own observations, confined to a strictly limited area of the arctic zone, may be briefly summed up as follows:

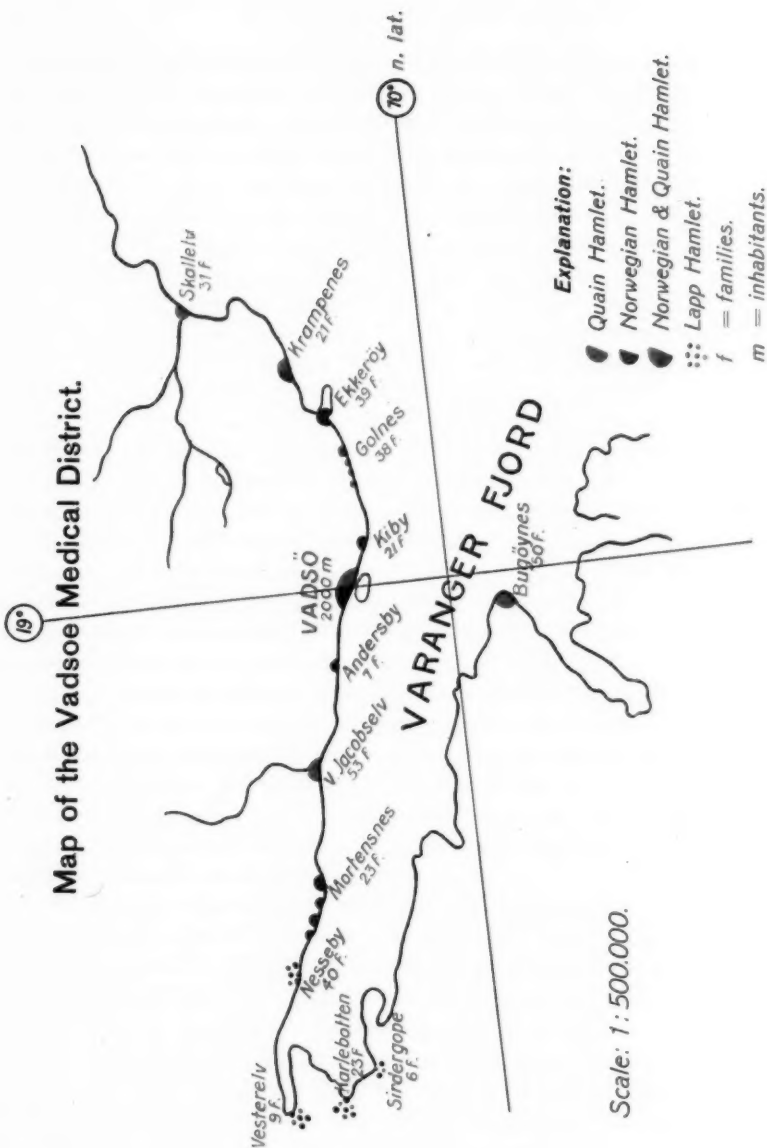
In my opinion, rickets is more prevalent in the Vadsoe district than in southern parts of the country. (On this point, my observations coincide with those of Dr. HARTMANN.) Considerable parts of the population benefit by an exceedingly liberal supply of vitamin D, while other parts (Skallelv, for instance) get only a — relatively, at least — small supply.

The fact that the district is situated so far north of the arctic circle greatly tends to reduce the influence of the light factor (considering the long period of obscuration, and the accompanying severe climate which compels the children to remain indoors). When, moreover, we consider that the value of the diet factor may lie below a reasonable minimum — as in the case of Skallelv — it is not to be greatly wondered at that rickets is such a frequently occurring disorder in these hamlets, nor that it presents so many severe cases.

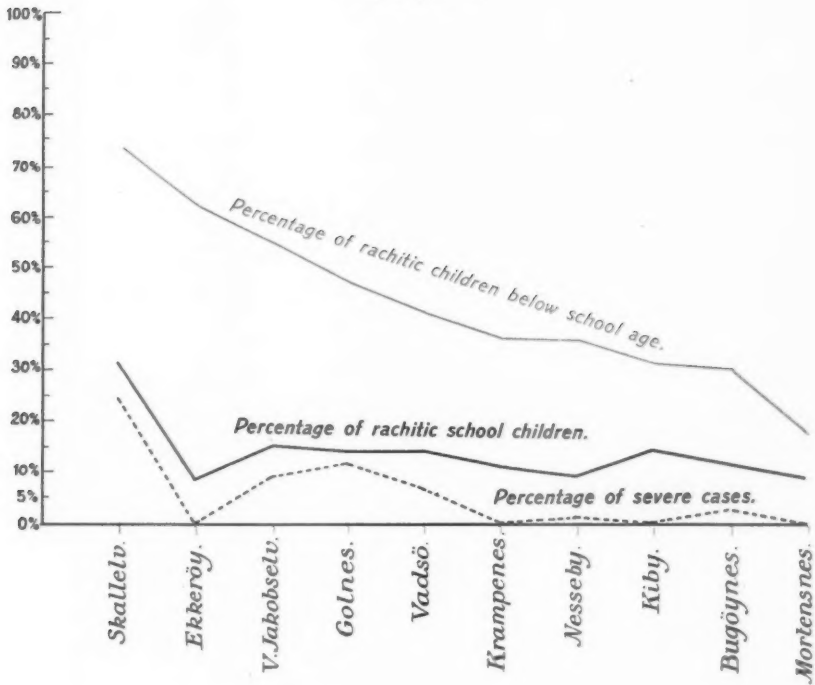
In hamlets having a large supply of vitamin D, rickets is, nevertheless, by no means a rarity, and this must, most probably, be due to a deficient light factor — a deficiency it would be hard to compensate for.

The very extensively adopted custom of bottle-feeding the infants has to be borne in mind and taken into due account.

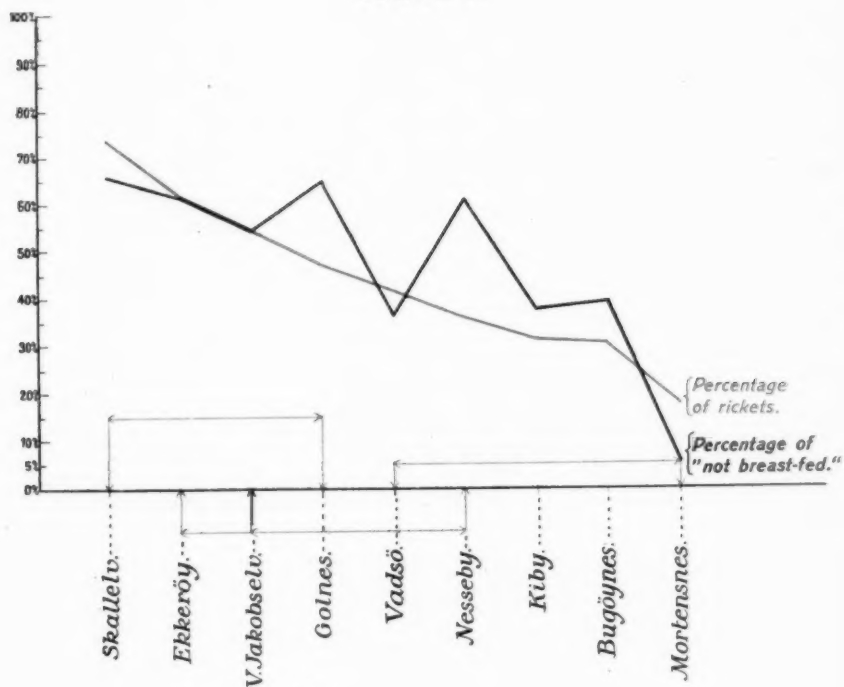
The high percentage of rickets at Skallelv — though including the breast-fed children of the hamlet — serves, nevertheless, to prove the great importance of the vitamin factor.



CURVE I



CURVE II





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BLOOD SUGAR

IN

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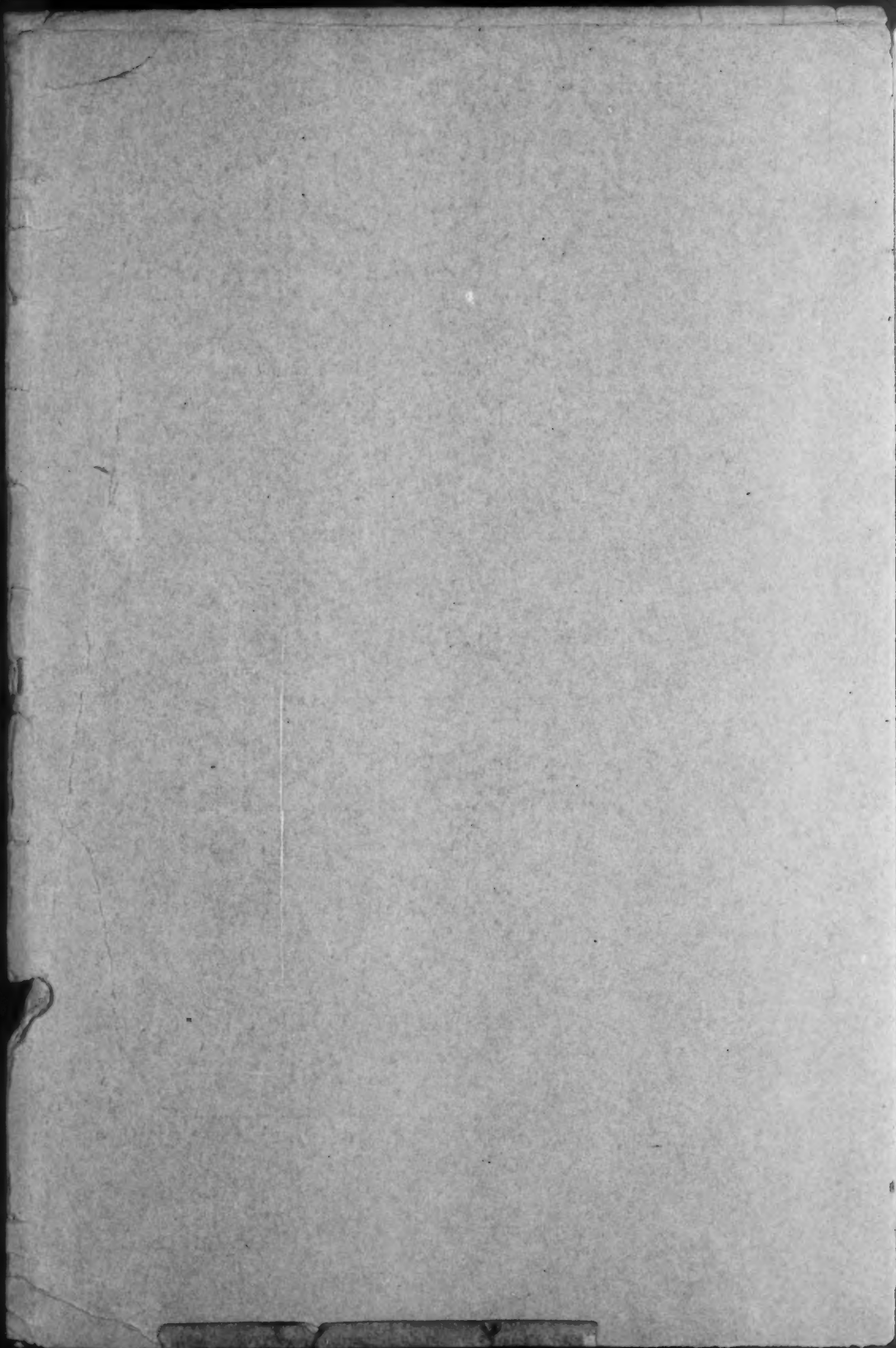
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BY

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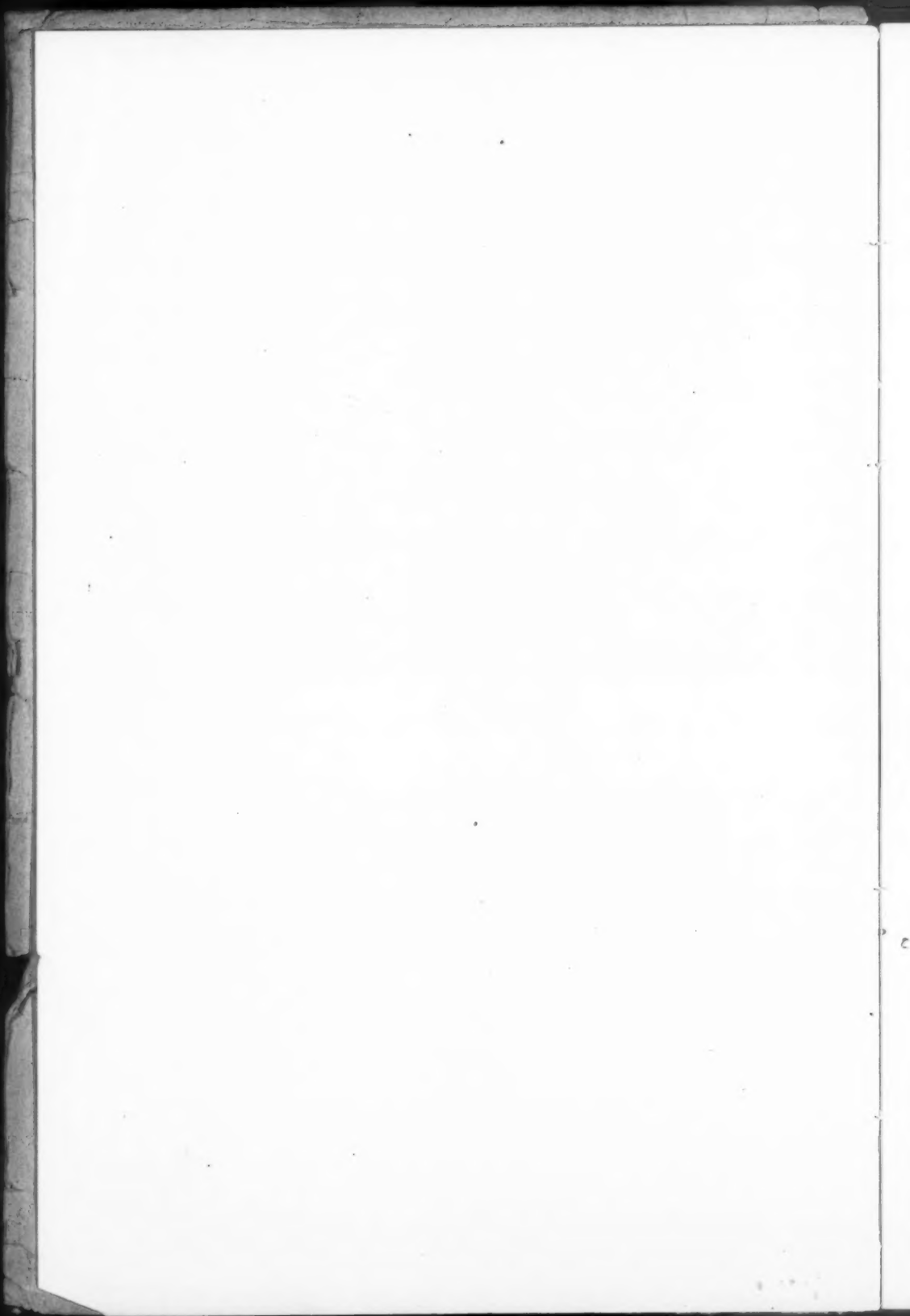
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WITH SPECIAL REFERENCE TO
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BLOOD SUGAR
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NORMAL AND SICK CHILDREN

WITH SPECIAL REFERENCE TO
COELIAC DISEASE

BY
ELISABETH SVENSGAARD



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PREFACE.

The studies reported in this paper*) were carried out during my engagement as Clinical Assistant in the Department of Pediatrics, the Rigshospital, University of Copenhagen.

I am greatly indebted to my chief, Prof. C. E. Bloch, for the good working years he has afforded me — and for his always encouraging interest in my work.

I further owe a debt of gratitude to Dr. H. C. Hagedorn for usefull instructions, and also to Dr. Paul Drucker for his ready assistance.

Finally I wish to give my thanks to the nurses of the department for their efficient help.

Some of the expenses connected with this work have been met with a grant from the P. Carl Petersen Foundation for which I give my thanks.

July 1931.

Elisabeth Svensgaard.

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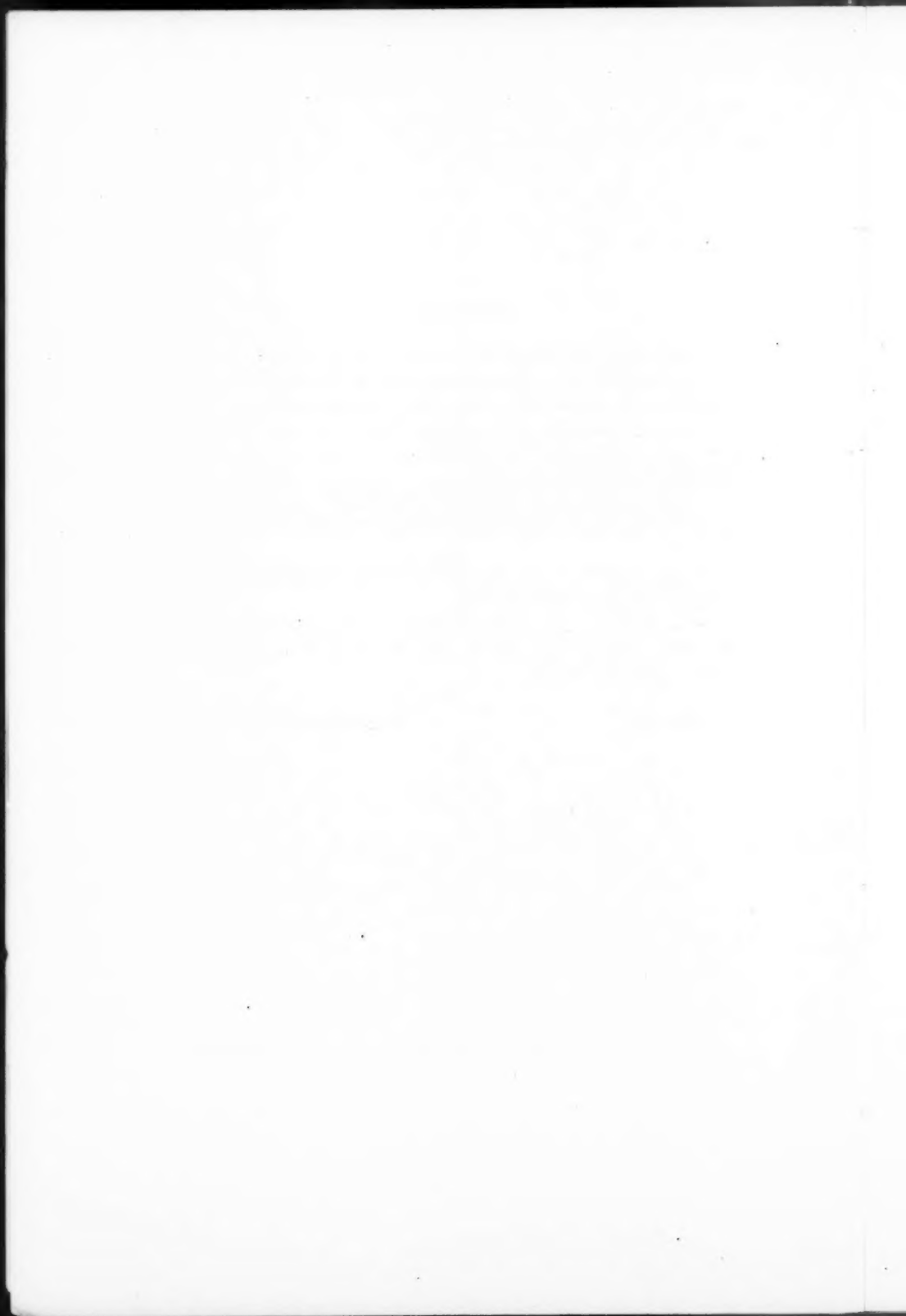


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INTRODUCTION.

Thorough investigations have been made into the blood sugar of adults under various conditions, especially after the micromethods for blood sugar determination had been devised. But, our knowledge of the blood sugar regulation in children is yet rather fragmentary, though several studies have been published on this subject in recent years; in particular the physiological variations are not sufficiently established. This entails an uncertainty in judging the analytic results when one is facing conditions assumed or asserted to be pathological.

As is well known, the vital phenomena in children differ on several points from the ones manifested by full-grown individuals — for one thing, they are much more unstable in children. This applies, for instance, to the heat regulation, the water metabolism, the acid-base equilibrium, etc. So it is not unreasonable to assume — as a working hypothesis — that something of that kind holds good of the carbohydrate metabolism too.

The studies presented in this work are aiming to fill out some of the gaps in our knowledge of the blood sugar regulation in healthy children, infants as well as older children; and to this purpose I have especially looked into the alimentary hyperglycæmia produced by ingestion of glucose.

In addition, I have examined the course of alimentary hyperglycæmia in various diseases in children.

For comparison with my blood sugar findings in children, I shall first give a brief survey of the prevailing views of the blood sugar in normal adults — here, too, with special reference to the alimentary hyperglycæmia after ingestion of glucose.

I. BLOOD SUGAR IN NORMAL ADULTS.

Survey of Prevailing Views with special reference to the Alimentary Hyperglycæmia after Ingestion of Glucose.

Most studies of the blood sugar in normal adults have been carried out on individuals from ca. 16 to ca. 40 years old. In Tables 1 and 2 (p. 12 and p. 19) I have entered the results from some of the most thorough investigations of recent years with the blood sugar determination made after the Hagedorn-Jensen method or after the Bang method, Table 1 dealing with the blood sugar in fasting individuals, Table 2 giving blood sugar findings after ingestion of glucose.

1. Fasting Blood Sugar Values. As a rule, the fasting values fall between 0.080 and 0.100 %, most frequently about 0.090 %, and only in rare instances outside the limits mentioned. In general, 0.110 % is taken as the upper limit of normal fasting values, but a few authors are inclined to raise this limit to 0.120 %. Values above 0.120 % are considered hyperglycæmic, and fasting values under 0.060 % are taken as hypoglycæmic.

It is a well known fact, however, that *the fasting blood sugar value is by no means constant from day to day* in the same individual. Czezowska & Goertz²¹ (1928) found variations in the blood sugar values of 4 fasting individuals, who were examined for 3 hours after they had been fasting 10–12 hours. In these examinations, blood was taken every half hour, and the blood sugar concentration was determined after

the Bang method. In one case, the authors found a rise of the fasting value amounting to 0.027 % in 90 minutes, and then a slow fall. In three other cases they found first a rise of the fasting value amounting to 0.012—0.016 %, and in the next hour a fall to 0.014—0.020 % below the initial value; at the end of the third hour, the curve had returned to the initial level. These variations were checked by a subcutaneous injection of atropin. The authors thought that psychic influence could be ruled out, as the experimental individuals were medical students, and the technique implied but a few pin pricks in the fingers. K. M. Hansen⁴⁵ (1923) took blood samples at intervals of 2 minutes, and found some very abrupt variations — e. g., between 0.076 % and 0.104 % within 4 minutes. She takes such »oscillations« to be characteristic of the blood sugar regulation mechanism. However, no similar findings have been obtained by other investigators who have taken blood samples at the same time intervals and have likewise employed the Hagedorn-Jensen method (Kjer⁶³ (1924), Jul Nielsen⁸⁰ (1928)).

Variations of the fasting blood sugar owing to psychic influence have been demonstrated by several investigators. Marañón⁷⁰ (1919) found an increase of the blood sugar in aviators immediately before and during their flying. Buc-ciardi¹⁷ (1928) made some tests on students, partly under psychic rest and partly under excitement (passing examination), and under the last condition he found a considerable increase of the fasting blood sugar value (up to 0.310 %). Bruusgaard¹⁰ (1929) found invariably an increase of the blood sugar in sportsmen under exertion; and he attributes this increase not only to the muscular work, but also to »emotional factors«. Other authors, on the contrary, have been unable to demonstrate any influence upon the fasting blood sugar value from anxiety. Thus, Epstein & Aschner²⁵ (1916) examined the blood sugar after 12—20 hours' fasting in surgical patients immediately before these were placed on the operating table, and they were never able to demonstrate any hyperglycæmia except in a few cases of hyperthyroidism,

hypertension, and other conditions where the rise of the blood sugar was attributable to other causes. Malmros⁷⁷ (1928) finds that emotion, fright or fear do not give rise to hyperglycæmia, and the same applies to mental overwork.

Table 1.
Fasting Blood Sugar Values in Normal Adults.

Author. Year of publicat.	Met- hod.	No. of persons exami- ned.	Age.	Fasting hours.	Blood sugar per cent.	
					Average.	Variations.
Jacobsen 1917	Bang	24	16-34	14-15	0.099	0.080-0.116
Löffler 1922	"		20-34	Night pause	0.096	
Punschel 1923	"	12	16-34	12	0.094	0.084-0.106
Malmros 1928	"	40	14-40	12	0.090	0.070-0.110
Hagedorn 1921	Hage- dorn- Jensen	20 (126 tests.)	18-62	14	0.089	0.062-0.109
Görtz 1927	"	14	17-48	14	0.092	0.085-0.104
Soisalo 1930	"	43 (100 tests.)	19-39	12	0.090— 0.099	0.060-0.116

2. *Alimentary Hyperglycæmia.* The rise of the blood sugar concentration after ingestion of glucose in doses of 50—100 gm., or after 1—2 gm. per kg. body weight, proceeds as a rule so that the blood sugar rises more or less abruptly and reaches its maximal value within $\frac{1}{2}$ —1 hour. In normal adults, up to middle age, the maximal value rarely exceeds 0.200 %, and it comes most frequently between 0.130 and 0.180 %. Then the alimentary hyperglycæmia subsides in the next 2—2½ hours; sometimes it takes a little longer, but, on the other

hand, often it passes even in less time. If the duration of the alimentary hyperglycæmia exceeds 3 hours, it is to be considered pathological.

A period of *hypoglycæmia*, i. e., a fall below the fasting blood sugar level, is very frequent after the alimentary hyperglycæmia is over (Jacobsen⁵⁶, Hagedorn⁴², Foster³⁰, Polak⁹⁵, Staub¹⁰⁷, Depisch & Hasenöhl²², Kylin⁶⁶, Steenström¹¹¹, Malmros⁷⁷, Soisalo¹⁰⁶, Meulengracht⁸¹). Often the hypoglycæmic values are obtained within a couple of hours after the glucose ingestion; and if the examination is extended over 3—4 hours, hypoglycæmic values are found in practically every instance. In general, this hypoglycæmia amounts to a blood sugar concentration 0.05—0.020 % below the fasting value. Meulengracht finds even a hypoglycæmic value as low as 0.63 % under the fasting value (fasting blood sugar value 0.100 %; minimum of blood sugar curve 0.037 %, 4 hours after ingestion of glucose); and in one case he finds a blood sugar value as low as 0.011 %. In 100 blood sugar examinations after glucose ingestion, Soisalo¹⁰⁶ finds in 84 instances hypoglycæmic values appearing within 2—2½ hours, sometimes even sooner (thus, he finds in one instance a blood sugar value of 0.058 % as early as 105 minutes after the glucose ingestion). Often he finds within the same period of 2½ hours a distinct rise of the hypoglycæmic part of the curve.

In older individuals the blood sugar values are a little different. Thus, some investigators find that the fasting values are higher after the age of 50 than before. Punschel⁹⁶ finds, for instance, that in the age of 58—91 years the fasting blood sugar values vary between 0.083 and 0.131 %, whereas his corresponding values in younger individuals vary between 0.084 and 0.106 %. Löffler⁷⁴ finds in the age 58—70 years an average fasting value of 0.106 %, whereas this average in the age 20—34 years (normal individuals) is 0.096 %. On the other hand, Lottrup-Andersen⁷², Malmros⁷⁷, and Hale-White & Payne⁴³ were not able to demonstrate any increase of the fasting blood sugar value in older indi-

viduals. But it is generally agreed that in old individuals the alimentary hyperglycæmia is more marked, both as to the maximal values obtained, and the duration of the hyperglycæmia. Values about 0.200 % (even up to 0.240 %) are thus encountered more frequently in older individuals than in younger, and in many instances the blood sugar curve does not return to the initial value within 3 hours (Lottrup-Andersen ⁷², Hale-White & Payne ⁴³, Löffler ⁷⁴, Malmros ⁷⁷, Punschel ⁹⁰).

As to the *influence of the preceding diet* upon the course of the alimentary hyperglycæmia, numerous investigators have demonstrated that a low carbohydrate, but high protein and fat, diet lowers the tolerance for subsequent carbohydrate supply, the result being a higher and more protracted hyperglycæmia than under ordinary conditions. Staub ¹¹⁰ found that this influence would manifest itself after 2 days of protein-fat diet, whereas the blood sugar curve would not be influenced when only the last meal before the examination had consisted of protein and fat. Similar results were obtained by Odin ⁹¹, Bergmark ⁶, Steenström ¹¹¹, Bornstein & Holm ¹¹, and Kageura ⁶¹. Kageura states that the decrease of carbohydrate tolerance which appears after 2 days of low carbohydrate diet keeps, on the whole, unaltered even though the low carbohydrate diet is continued for some time; on addition of carbohydrates to the diet, the assimilation power is restored fairly rapidly. In self-experiments, Odin ⁹¹ finds, on the contrary, that the tolerance may be reduced for some time (several weeks). Malmros ⁷⁷ has made a thorough study into this question, and he confirms the finding that there is an increase in the sensitiveness to carbohydrates after a few days of low carbohydrate diet. He demonstrates that this hypersensitiveness is not due to a ketosis, as has been stated by some authors. He has further established that it does not make any difference in the course of the alimentary hyperglycæmia whether the preceding diet

is composed of ordinary mixed food or an abundance of carbohydrate.

Also the *preceding fasting period* has an influence on the blood sugar regulation. Staub¹⁰⁸ has made some thorough investigations into this question. His experimental individuals, who were 20—40 years old, were fasting up to 2 days, and during this fasting period, Staub studied the alimentary blood sugar rise after ingestion of glucose at intervals of 5—12 hours. Thus he was able to distinguish between 2 fasting periods: a first period — up to 10—15 hours after the last meal — which he calls relative inanition, and a second period — the rest of the examination period — which he designates as absolute inanition. Ingestion of glucose in the first hours of the relative inanition and during absolute inanition gives a greater blood sugar rise than does glucose ingestion in the last part of the relative inanition, i. e., after 10—15 hours' fasting. Traugott¹²² made some experiments on himself with ingestion of the same dose of glucose after an ordinary fasting period (night pause) and after 3 days of absolute inanition, and he found that the blood sugar increase was 4 times higher under the last conditions than under the first. Staub (109) explains these findings as follows: »Nach Kohlenhydratkarenz oder Kohlenhydratarmut im Organismus besteht eine relative Insuffizienz der Fermentfunktionen, es besteht ein Mangel an wirksamen spezifischen »Assimilationsfermenten«.

The course of the alimentary blood sugar curve is influenced not only by the preceding fasting period and the nature of the diet, but also by the condition of the individual during the functional test itself. This has been emphasized in particular by Hagedorn⁴², who finds that *muscular activity* during the functional test causes the blood sugar curve to be lower than in rest, whereas vigorous exertion before the test has no influence upon the course of the alimentary hyperglycaemia. Similar findings have been reported by Staub¹⁰⁹ and by Bornstein & Holm¹¹.

Henry John⁵⁰ finds that *nausea* during the test gives

a decrease of the alimentary hyperglycæmia. The same is reported by Hale-White & Payne⁴³.

As to the relation between the degree of hyperglycæmia and the amount of glucose ingested, several authors have found that *different doses of glucose* may give the same degree of hyperglycæmia. Jacobsen⁵⁰ found uniform increases after 25, 50 and 100 gm. glucose. Also Hagedorn⁴² came to the result that there is no direct proportion between the degree of hyperglycæmia and the amount of glucose ingested. Traugott¹²⁹ observed that the blood sugar value might rise to the same height after 20 as after 60 and 100 gm. glucose. This question has been studied in particular by K. M. Hansen⁴⁵ who gave each person glucose in doses varying between 20 and 400 gm., and found the upper limit of the blood sugar rise in normal adults to be about 0.180 %. She concludes:

»In normal persons there is an upper limit for the rise in the level of the blood sugar after glucose administration. This limit perhaps varies a little in different persons but hardly exceeds 0,18 %.

»The explanation that the blood sugar rise ceases in the neighbourhood of 0.18 % must be sought in the phenomenon which is called removal-acceleration, by which is understood the power the organism possesses of accelerating the removal of sugar from the blood-stream to a practically unlimited extent at this concentration, from blood as it is obtained from the lobe of the ear. The concentration at which this power reaches its full capacity is called the optimal concentration. The power of acceleration is perhaps due to an increased supply of the pancreas hormones to the blood.

»The total rise of the blood sugar curve after the administration of glucose varies within very narrow limits depending upon the organism's condition when the dose is above a certain size, with smaller doses changes in the organism's condition have a more marked effect.

»When the dose is greater..... no proportion whatever can be shown to exist between the size of the dose and the height of the total-rise.«

It should be mentioned, however, that when K. M. Hansen gives glucose in very large doses — 250 gm. or more — the blood sugar curve stays at a high level much longer than when glucose is given in moderate doses, even though the maximal value does not come above 0.18 %; and although with these large doses of glucose the hyperglycæmia has fallen off considerably after two hours, it does not return within this length of time to the level of the fasting blood sugar as is usually the case after moderate doses of glucose.

The blood sugar rise after *very small amounts of glucose* has been examined by Staub¹⁰⁷, who showed that a dose, for instance, of 10 gm. glucose in adults gives but a slight and brief rise of the blood sugar level. Malmros⁷⁷ found likewise a slight rise of the blood sugar after ingestion of $\frac{1}{3}$ gm. glucose per kg. of body weight; but after $\frac{1}{2}$ gm. per kg. he found the blood sugar rise upon the whole to be just as marked as after 1 gm. per kg.

Traugott¹²² has looked into the behaviour of the blood sugar after *repeated ingestions of glucose within a short time*. First he gave 20 gm. glucose, then — at intervals of $\frac{1}{2}$ —2 hours — 3 times 20 gm. glucose, and finally, 4 hours after the first dose, 100 gm. glucose, that is, a total of 180 gm. In these experiments he found, that in normal individuals hyperglycæmia was produced only by the first dose of 20 gm. glucose while the subsequent doses had no effect (in diabetics, on the other hand, he found a new rise of the blood sugar after each dose). He says: »Aus unseren Versuchen geht hervor, dass die erste Dextroseabgabe die Leberzellfunktion derart beeinflusst, dass eine Mehrleistung der Zelle bezüglich der weiteren Zuckerverwertung resultiert.« Foster³⁰ has confirmed the findings of Traugott, but many other investigators have not been able to agree with him, as they found a new rise of the blood sugar after each dose of glucose in non-diabetics too (Holst⁵⁴, Malmros⁷⁷, Barrenscheen & Eisler³).

It has been demonstrated repeatedly, e. g., by Hale-White & Payne⁴³, Foster³⁰, and Malmros^{77,78} that the

hyperglycaemia subsides even when glucose is present yet in the stomach, or while glucose in all probability is still being absorbed from the intestinal canal. When Malmros gave a highly concentrated solution of glucose (e. g., 50 %), he was able to withdraw considerable amounts of glucose from the stomach 2 hours after the ingestion, although the blood sugar concentration had returned to the fasting level. The subsequent course of the blood sugar curve was not influenced by the withdrawal of the glucose remaining in the stomach. Nor is the blood sugar curve influenced to any noticeable degree by differences in the concentration of the glucose solutions ingested (Hagedorn⁴², Malmros⁷⁷). Apart from this, it has been found that a glucose solution of ca. 10 % is apt to leave the stomach more rapidly than solutions of higher or lower concentration, and that concentrated glucose solutions are diluted with fluid given off into the stomach. (Beeler, Bryan, Cathcart & Fitz⁵).

By examination of the *blood sugar curve after glucose ingestion in the same individual on different days* one does not obtain identical hyperglycæmic curves but greater or smaller variations from day to day (Jacobsen⁵⁶, Staub¹⁰⁷, Hale-White & Payne⁴³, Hagedorn⁴², Jul Nielsen⁸⁶, Soisalo¹⁰⁸, et al.).

In normal adults under the same experimental conditions, Hagedorn⁴² found that the maximal values of alimentary hyperglycaemia might vary as much as 0.047 %; as a rule, however, the individual variations were considerably smaller. The duration of the alimentary hyperglycaemia could vary in the same individual as much as 45 minutes.

Soisalo¹⁰⁸ has tried out whether it might be possible by *standardization of the diet* to obtain uniform blood sugar curves in the same individual on different days after ingestion of the same amount of glucose. (The standard diet consisted in ordinary mixed diet, with the various food elements weighed off in definite amounts. Salt and pepper were not weighed. Water was given ad libitum, up to 1200 cc.). He found that sometimes the curves were almost identical within the limits

Table 2.
Blood Sugar Values after Glucose Ingestion in Normal Adults.

Author. Year of public.	Method.	No. of persons exam.	Age.	Fasting hours.	Fasting blood sugar value %	Dose of glucose.	Maximal blood sugar value %	Time of maximal value after glucose ingest.	Duration of ali- ment. hyper- glycæm.	Time interval between blood samples
Jacobsen 1917	Bang	23	16-34	2-4½ after small morning meal	0.099	100 gm. in 200 cc water	17 cases: 0.110- 0.189. 6 cases: 0.190- 0.227.	¼-1 hour.	1-2½ hours.	15 min. in 1' hour; then ½-1 h.
Malmros 1928	Bang	39	14-40	12	Av.: 0.090 Var.: 0.070- 0.110	1 gm. in 10 % sol. per kg. body weight	32 cases: 0.130- 0.180. 7 cases: 0.180- 0.200.	Less than 1 h.	ca. 2 h.	5-10 min in 1' hour; 10-15 min. in 2' hour; then ½ h.
Hagedorn 1921	Hage- dorn- Jensen	20 (39 tests.)	18-62	14	Av.: 0.086 Var.: 0.070- 0.105	1 gm. in 10 % sol. per kg. body weight	0.121- 0.189, 2 tests. 0.201- 0.214.	½-1 hour.	Less than 2½ h.	15 min.
Soisalo 1930	Hage- dorn- Jensen	43 (100 tests.)	19-39	12	Av.: 0.090- 0.099	1 gm. in 10 % sol. per kg. body weight	72 exams.: 0.130- 0.179. Var.: 0.117- 0.207.	¼-1 hour.	Less than 2½ h.	5-15 min. in 1' hour; then ½ h.

of experimental error, but in other instances the curves showed rather wide variations with regard to the maximal value and duration of the hyperglycæmia. The greatest difference between the maximal hyperglycæmic values recorded in the same individual on different days was 0.052 %, with a difference of 5 minutes in their respective time of appearance. The greatest difference of the maximal values in their time of appearance in the same individual was 15 minutes; and the greatest difference in the duration of the hyperglycæmic periods in the same individual was 1 hour. Thus he found that uniformity of experimental conditions does not do away with variations in the blood sugar curves of the same individual. He found, moreover, that in glucose ingestion tests it is not necessary to standardize the diet; for the blood sugar curves obtained in persons on ordinary mixed diet are just as reliable for estimation of the blood sugar regulation as are the blood sugar curves obtained in persons on a standard diet.

II. BLOOD SUGAR IN NORMAL CHILDREN.

A. PREVIOUS INVESTIGATIONS.

1. Fasting Blood Sugar Values.

The results reported from previous studies on the blood sugar in children are rather conflicting, but the divergence may be largely attributable to the marked differences in the technique employed by the various authors.

In surveying the fasting values observed in children we find the reported averages to vary from 0.074 % (Lucas⁷³) to 0.103 % (Bing & Windelöw⁸); and in looking for a reasonable explanation of the wide divergence of the averages reported, we find that *the blood sugar tests have been made at times that differ in relation to the meals*. Several investigators have taken a fasting period of only 3½ hours or less. This applies, for instance, to Bing & Windelöw⁸ (1913), who examined the blood sugar in 15 children and found the average fasting value to 0.103 %, with variations from 0.071—0.131 %. Heller⁴⁸ (1916) examined the blood sugar concentration ¼—3 hours after a meal and found the values varying between 0.066 and 0.133 %. On going through his protocols, however, it will be noticed that all his values above 0.100 % have been obtained within 2 hours after a meal (he does not give the nature and quantity of the meal). In 1913, Goetzky³⁸ made a number of blood sugar examinations on 100 children, aged from 1 day to 13 years. He thinks that the blood sugar concentration increases with the age; but often he makes the examination ½—1 hour after a meal, and this explains why, for instance, he in children of 1—12 years finds an average fasting

value of 0.102 %. Taking into account only the values he obtained 4 hours after a meal, the average fasting value is 0.077 %. In children, after 3 hours' fasting, Lindberg⁷¹ (1917) found the average blood sugar value to be 0.111 %, the extremes 0.087 and 0.124 %.

In compiling the blood sugar values obtained in children who have fasted but 3½ hours or less, one will notice that the values are often above 0.100 %; but, on the other hand, there are also a good many values that come within the established fasting values of adults — i. e., 0.090 % and there about.

If now we turn to the blood sugar values obtained after a fasting period of 4 hours or more, the results are different. In Lindberg's⁷¹ material, for instance, the children who have been fasting 12 hours show an average blood sugar value of 0.096 % and variations from 0.077 to 0.107 %. Niemann⁸⁷ (1916), who obtains about the same results whether the children are fasting 4 or 8 hours, finds an average blood sugar value of 0.079 % in variations from 0.070 to 0.086 %. Mertz & Rominger⁸⁰ (1921) find after 4 hours' fasting an average value of 0.081 % in variations from 0.060 to 0.101 %. In infants fasting 4—6 hours, Rumpf⁹⁰ (1924) finds the blood sugar values varying from 0.071 to 0.089 %, with an average of 0.076 %; in children of 3—7 years he finds an average of 0.085 %, and at the age of 10—14 an average of 0.091 %. The above-mentioned authors have all employed the Bang method.

Sedgwick & Ziegler¹⁰⁵ (1920), using the Folin method, find in breast-babies after a »night pause« (no feeding during the night) an average fasting value of 0.08 % and variations from 0.05 to 0.11 %. Lucas⁷³ (1921), who is also using the Folin method, finds after 4 hours' fasting an average blood sugar value of 0.074 % in variations from 0.051 to 0.099 %. Tisdall, Drake & Brown¹¹⁷ (1925), who employ a modification of the Schaffer-Hartmann method, find an average fasting value of 0.085 % in variations from 0.058 to 0.109 %. There are, finally, two reports on fasting blood sugar values

in children determined after the Hagedorn-Jensen method — the same method as is employed for the examinations reported in this paper: Schiff & Coremis¹⁰² (1926) examine the blood sugar in 21 infants after 4 hours' fasting and find the average value to be 0.09 %. Herlitz⁵⁰ (1928) examines the blood sugar after 5 hours' fasting in 40 normal breast-babies (2—8 months old) and in 30 normal bottle-babies (2—8 months); in the first group he finds an average value of 0.088 % in variations from 0.077 to 0.099 %, in the latter group the average value is 0.086 % and the variations 0.071—0.103 %.

From these findings it is evident that, *when children have fasted 4 hours or more, their blood sugar values approach the fasting values usually obtained in adults, but, on the whole, the values appear to be a little lower in children than in adults; in adults the fasting values come most frequently to 0.090 % or a little more, whereas in children they fall as a rule below 0.090 %, about 0.080—0.085 %.*

Table 3 (p. 26—27) gives the results obtained by various investigators with regard to the fasting values of the blood sugar in normal children.

Crevelde²⁰ (1929) has examined the blood sugar in *premature children* (Hagedorn-Jensen method). His material comprises 60 children under 2 months with a birth weight of less than 2500 grams. But he does not give the weight of the children at the time of the blood sugar examination. After a fasting period of 4—5 hours he finds the blood sugar values varying between 0.030 and 0.070 % — that is, *very low values*.

Several authors have looked into the *behaviour of the blood sugar through a protracted fasting period — one or several days*. The results of these investigations are somewhat divergent, however, some authors stating that the blood sugar concentration falls considerably after a fasting period of 24 hours, for instance, whereas other authors find that the fasting blood sugar values stay a long time — even as long as 60 hours — at approximately the same level. Mogwitz⁸⁴ (1913) has thus made 3 fasting experiments in which the children had the usual amount of fluid in form of saccharin water, and nothing

else. The results of these tests show that inanition for 24 hours or more is followed by a slow fall of the blood sugar concentration, from initial values of 0.07—0.11 % to values as 0.057, 0.056 and 0.047 %. But his findings show, too, that the fasting values may stay at the same level through the first 24 hours; after this, they begin to go down slowly.

Lindberg⁷¹ (1917) has made similar hunger experiments of 60 hours' duration, on children of 3—9 months. He took blood samples at intervals of 12 hours; but he did not find any particularly marked decrease in the blood sugar concentration. Thus, for instance, after 12 hours' fasting the blood sugar values varied from 0.077 to 0.107 %, with an average of 0.096 %. After 24 hours' fasting the average value was 0.074 %; after 36 hours 0.073 %; after 48 hours 0.074 %; and after 60 hours it was still 0.074 %.

Rumpf⁹⁹ (1924) uses two designations for the fasting blood sugar values: »fasting value« and »hunger value«. »Fasting value« applies to a blood sugar concentration of 0.070—0.090 %; »hunger value« means a blood sugar percentage less than 0.070. He finds only »fasting values« when the blood is examined 4—5 hours after a meal, but »hunger values« — e. g., 0.056 — may appear as early as 7 hours after a meal. At other times he has observed that the blood sugar concentration may stay at the same level even through a protracted fasting period — e. g., 27 hours. He thinks that the poorer the nutrition of the child, the more rapidly falls the blood sugar concentration.

Schiff & Coremis¹⁰² (1926) have examined the blood sugar in infants under 24 hours' fasting with fluid intake. They find that under these conditions the blood sugar will fall on an average to about one half of the fasting value. For instance, after 4 hours' fasting they find an average value of 0.090 %, after 24 hours' fasting an average value of 0.038 %, with respective variations of 0.080—0.105 % and 0.031—0.053 %. When the fluid supply is given in form of 10 % rice water, they find similar values of blood sugar concentration; but the addition of 8 % cane sugar is enough to keep the blood sugar concentration from falling to the low values. They have

made some other tests, in which the children are fasting 24 hours without getting an adequate supply of fluid, and here they observe the peculiar phenomenon, that the hunger hypoglycæmia does not appear. In this connection Schiff & Coremis point out that in infants with toxic infectious gastro-enteritis — so-called toxicosis — which involves a great loss of water, the blood sugar concentration is normal or even increased, the inanition notwithstanding. This observation has been confirmed by Mogwitz⁸⁴, Fedynski, Poltiewa & Wilenskaja²⁸, and Nystén⁹⁰.

Gilchrist³⁰ (1929), who employs the Mc. Lean method, states that the duration of the fasting has no influence upon the level of the fasting blood sugar concentration. But in her tests the longest fasting period was only 15 hours. She finds an average value of 0.106 % after 8 hours' fasting and 0.107 % after 15 hours' fasting, with variations from 0.067 to 0.166 %. It is rather difficult to see any reason for these high values which are above the values obtained by other investigators. Schönfeld¹⁰⁴ (1930) examined the blood sugar in 80 infants after 4, 10 and 12 hours' fasting. During these fasting periods the children were getting their usual supply of fluid. He found that in the majority of cases the blood sugar value was lowest after the long fasting period, although in a good many instances the blood sugar value was approximately the same after 4 hours' fasting as after 10—12 hours' fasting. In contrast with Rumpf, he did not find any relation between the blood sugar fall and the nutrition of the individual.

As to the *emotional influence upon the blood sugar in fasting children*, there have been found no variations that may be set down under this heading. Mogwitz⁸⁴ has examined the blood sugar of the same child under complete rest and under violent excitement, without being able to demonstrate any difference in the blood sugar concentration on the two occasions. Also Rumpf⁹⁹ finds that the blood sugar values stay within the physiological limits under exaltation, screaming and crying. Oppel & Fedorow⁹² examined through 3 hours the blood sugar in children who had been fasting for 15

Table 3.
Fasting Blood Sugar Values in Normal Children.

Author, Year of publication.	Method.	No. of persons examined	Age	Fasting hours	Blood sugar per cent.	
					Average	Variations
Bing & Windelöw 1913	Bang	15	1-13 m.	3½	0.103	0.071-0.133
Götzky 1913	"	100	1-12 d.	1½-4	0.085	
			1-12 m.	"	0.095	
			1-12 y.	"	0.102	
			1-12 y.	4	0.077	
Mogwitz 1913	"	29	7 h.-3 y.	3½-4	0.090	0.07-0.11
Heller 1916	"	15	5½ h.-9 d.	¼-3		0.066-0.133
Niemann 1916	"	26	3 w.-9 m.	4-8	0.079	0.070-0.086
Lindberg 1917	"	18	3-9 m.	3 12	0.111	0.087-0.124
					0.096	0.077-0.107
Frank & Mehlhorn 1920	"	72	1½-3 y.	?	0.086	0.066-0.108
Mertz & Rominger 1921	"	17	1 w.-1 y. + 1 w.	4	0.081	0.060-0.101
Nystén 1921	"	21	1 d.-1 y.	3½	0.107	0.085-0.128
Rumpf 1924	"	150	Infants 3-7 y. 10-14 y.	4-6	0.076	0.071-0.089
		10			0.085	0.074-0.107
		35			0.091	0.078-0.102

Table 3 cont.).

Author. Year of publication.	Method.	No. of persons examined.	Age	Fasting hours	Blood sugar per cent.	
					Average	Variations
Fedynski, Poltiewa & Wilenskaja 1926	Bang, Hagedorn- Jensen	35	?	?	0.081	0.040—0.125
Schiff & Coremis 1926	Hagedorn- Jensen	21	Infants	4	0.090	0.08—0.105
Herlitz 1928	Hagedorn- Jensen	40 Breastbabies 30 Bottlebabies	2—8 m 2—8 m	5 5	0.088 0.086	0.077—0.099 0.071—0.103
Sedgwick & Ziegler 1920	Folin	50 Breastbabies	3—43 d.	Night pause	0.08	0.05—0.11
Lucas 1921	"	?	0—12 d.	4	0.074	0.051—0.099
Greenwald & Pennel 1930	"	49	1—10 d.	3	0.076	0.060—0.100
Brown 1924	Mac Lean	35	Few h. — 1 y.	3—4	Under 2 w.: 0.087 Over 6 w.: 0.106	0.072—0.097 0.086—0.116
Mac Lean & Sullivan 1929	Lewis-Benedict Myers-Bailey's modific.	13	5 w. —2½ y.	3½—4	0.096	0.080—0.110
Tisdall, Drake & Brown 1925	Schaffer- Hartmann (modific.)	68	1—18 m.	4	0.085	0.058—0.109

hours before the examination. 300 cc. of water was given, without addition of sugar. They found no particular variations in the blood sugar concentration, and they found it therefore warrantable to rule out any influence of emotional hyperglycaemia produced merely by the taking of blood samples.

2. Behaviour of Blood Sugar after Ingestion of Glucose.

I shall now briefly outline the results obtained by various investigators with regard to alimentary blood sugar curves in children, leaving out the examination made on venous blood (e. g., the findings of Flood²⁰, Duzár & Hensch²⁴, Mac Lean & Sullivan⁷⁵).

I am leaving out the latter group of investigations, because it has been demonstrated by animal experience (Henriques & Ege⁴⁰) and by examinations on normal adults (Hagedorn⁴², Holst^{54,55}, K. M. Hansen⁴⁶, Depisch & Hasenöhr²², Rosenow⁹⁸, et al.) that after glucose ingestion the blood sugar concentration is higher in capillary and arterial blood than in venous blood. Thus, Hagedorn⁴² finds differences after glucose ingestion as great as 0.038 %, and Holst⁵⁴ finds differences up to 0.057 %. Rosenow⁹⁸ has examined the blood from the medial artery and the median vein of the cubitus in 14 normal individuals, and he finds the glucose content of the arterial blood to be higher than that of the venous blood in fasting as well as after glucose ingestion. In fasting the difference was up to 0.029 %, after breakfast it was 0.032—0.053 %.

Blood sugar studies on children after glucose ingestion have been carried out with techniques differing so much that it is difficult to deduct some common features from the results. Several investigators have taken the blood samples only at intervals of $\frac{1}{2}$ hour or more, which naturally gives but a most deficient picture of the course of the blood sugar curve. This applies, for instance, to the studies reported by Mertz & Ro-

mingers⁸⁰ (1921). These authors made their investigations on infants, the blood sugar determination after the Bang method, implying a dose of 30 gm. glucose in 100 cc. water (in some cases 50 gm.), which means that the amount of glucose ingested varied between 3.4 and 15 gm. per kg. of body weight. In their conclusions they give their highest maximal blood sugar value as 0.208 %, and the average maximal value as 0.128 %; but thereby they leave out of account one case in which the maximal value was 0.295 %, and another case in which it was 0.261 % (in these cases the respective doses of glucose were 14 and 9 grams per kg. of body weight). They conclude: »dass im allgemeinen die pro Kilogramm gegebene Menge nicht in gesätzmässige Beziehung zum absoluten Anstieg der Blutzuckerkurve zu bringen ist, soweit nämlich der Unterschied der Zuckergaben nur einige Gramm pro Kilogramm Körpergewicht beträgt.«

Goetzky³⁰ (1921) gives 2—3 gm. glucose per kg. in 10 % solution (Bang method). He finds maximal values varying between 0.150 and 0.200 % within 1 hour after the glucose ingestion. After 2 hours, the blood sugar curve has returned to the initial level.

Rumpf⁹⁰ (1924) examines infants with 1.3 gm. glucose in 10 % solution per kg. (Bang method). In the first hour he takes blood samples every 5—10 minutes, in the next every 10—15 minutes, and in the third hour every 30—60 min., and finds on an average a maximal blood sugar rise of 0.051 % in about $\frac{1}{2}$ hour. The highest rise amounts to 0.081 %, reached in 40 minutes. The blood sugar concentration returns again to fasting values within ca. $2\frac{1}{2}$ hours.

Muriel Brown¹⁴ (1928) gave 1 gm. glucose per kg. of »expected« body weight, after 3—4 hours' fasting, to 10 normal children varying in age from 6 days to 13 months. Blood was taken every $\frac{1}{2}$ hour for 2 hours. The blood sugar rise was usually completed within $\frac{1}{2}$ hour. The maximal values varied between 0.120 and 0.156 %. (Mac Lean method).

Herlitz⁵⁰ (1928) examined 21 children, from 6 weeks to 10 months old, after 5 hours fasting (Hagedorn-Jensen method). He gave 1.3 gm. glucose per kg., and took blood samples

$\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$, 1, $1\frac{1}{2}$, 2, 3, 4 hours after ingestion of glucose. The average maximal value was 0.123 % in variations from 0.110 to 0.162 %. The maximal values were reached within $\frac{1}{2}$ —1 hour, and the curves returned to the fasting level within 3 hours after the glucose ingestion.

In addition to these examinations, Herlitz⁵⁰ made a series of tests on 14 children, 3—11 months old, with a dose of 4—7 gm. glucose per kg. in 100 cc. water. The highest maximal value recorded in these tests was 0.242 % (after ingestion of 5 gm. glucose per kg.); the lowest maximal value was 0.135 % (after 6 gm. glucose per kg.); the average of the maximal values was 0.183 %. The duration of the hyperglycæmia was the same as in the examinations with smaller doses. Herlitz finds that the alimentary hyperglycæmia is followed by hypoglycæmia less frequently in infants than in adults. From his findings he concludes (⁵⁰, p. 37): »Zusammenfassend dürfte man die Resultate der vorgelegten Untersuchung als starke Stütze für die Annahme bezeichnen können, dass die Insulinproduktion, die nach peroraler Verabreichung sehr grosser Glykosedosen bei gesunden Säuglingen im Alter von 3—11 Monaten ausgelöst wird, meist gut mit derjenigen vergleichbar ist, die man unter analogen Verhältnissen bei Erwachsenen erhält. In 3 von den 14 untersuchten Fällen wurde jedoch beobachtet, dass die Blutzuckersteigerung nach peroraler Verabreichung so grosser Glykosedosen an gesunde Säuglinge auffallend stark war im Vergleich zu dem gewöhnlich bei Erwachsenen gefundenen Verhalten, und ferner war die »hypoglykämische Phase« in allen untersuchten Fällen nur angedeutet.«

Still, it seems to me, the figures of Herlitz do rather suggest that the size of the dose is of greater significance to the blood sugar concentration in children than is the case in adults. For, with a few exceptions, the maximal blood sugar values after the large doses of glucose come far above the maximal values observed after ingestion of only 1.3 gm. glucose per kg.

Greenwald & Pennel³⁷ (1930) examined the blood sugar (Folin method) in 15 normal new-born, 2—10 days old, after

3 hours' fasting by giving 2 gm. glucose per kg. of body weight. Samples of blood were taken only $\frac{1}{2}$ —1—2 hours after ingestion of glucose. In all the cases excepting one, there was a rise of the blood sugar concentration within $\frac{1}{2}$ —1 hour, reaching on an average a maximal value of 0.112—0.115 %; in 3 cases the maximal value was about 0.150 %. As a rule, the blood sugar values would again return to the fasting level within 2 hours. The authors conclude: »The sugar tolerance curve is essentially the same as in older infants and adults except that the curve is at a lower level.«

Inger Jensen⁵⁸ (1930) has studied the blood sugar in 14 boys, 8—11 years old, with a special view to the maximal height of the rise in alimentary hyperglycæmia. She gave 1 gm. glucose per kg., in 15—20 % solution. The maximal values varied between 0.098 and 0.189 %, and appeared on an average within 80 minutes after the glucose ingestion. In many of the tests she found relatively low maximal values; but she mentions herself that the boys did not rest completely during the examination periods, but were allowed to walk about in the room; and this may explain the low values in some of the tests.

In 1925, Tisdall, Drake & Brown¹¹⁷ reported investigations into the hyperglycæmic blood sugar curve in infants; but as these studies were made with subcutaneous and intravenous injections of glucose, they will not be considered in this connection.

As will be noticed, *only Rumpf⁹⁹ and Herlitz⁵⁰ have taken blood samples from infants at intervals of $\frac{1}{4}$ hour or less.* Both authors have given 1.3 gm. glucose per kg. of body weight, in 10 % watery solution. Rumpf, employing the Bang method, finds an average maximal value of 0.130 % in a total of 80 tests, in which the rise varies from 0.024 to 0.081 % above the fasting value. Herlitz, using the Hagedorn-Jensen method, finds an average maximal value of 0.123 % in 21 tests, with variations from 0.110 to 0.162 %. *In children under one year, then, these two authors have found the rise of the blood sugar concentration in alimentary hyperglycæmia to come within the same limits as are observed in adults. The*

Table
Blood Sugar Values after Glucose

Author. Year of public.	Method.	No. of per- sons- exa- mi- ned	Age.	Fa- sting hours	Fa- sting blood sugar value ‰	Dose of glucose
Mertz & Rominger 1921	Bang	17	7 days to 1 y. 7 d.	4	0.081	Regardless of age and weight: 30 gm.—50 gm. gluc. in 100 cc. water, i. e., 3—15 gm. per kg. body wt.
Goetzky 1921	"	?	Infants	4—5	?	2—3 gm. gluc. in 10 ‰ sol.
Rumpf 1924	"	80	Infants	12—13	0.079	1.3 gm. gluc. per kg. body wt. in 10 ‰ sol.
Herlitz 1928	Hage- dorn- Jensen	21	1 $\frac{1}{4}$ -10 m.	5	0.085	1.3 gm. gluc. per kg body wt. in 10 ‰ sol.
Herlitz 1928	"	14	3-11 m.	5	0.086	4—7 gm. gluc.

maximal values appear within $\frac{1}{2}$ —1 hour, and the duration of the alimentary hyperglycæmia is less than 3 hours.

Table 4 gives an abstract of the results obtained by various investigators with regard to blood sugar values after ingestion of glucose.

The influence of protracted fasting upon the alimentary hyperglycæmia in children has been examined by Lindberg⁷¹. In some tests he gave the individual a meal after 60 hours' fasting, and 7 hours after this meal he found a blood sugar value of 0.144 %, while 10 hours after the meal the blood sugar value was 0.115 % — that is, the test showed hyperglycæmic values at times when one will usually find fasting values. Schiff & Coremis¹⁰² gave 2 gm. glucose per kg. of body weight, dissolved in 50—60 cc. water, after 24

4.

Ingestion in Normal Children.

Maximal blood sugar value ‰	Time of maximal value after glucose ingest	Duration of alimentary hyperglycaemia	Time interval between blood samples
0.071—0.128 above fasting value	$\frac{1}{2}$ —1 $\frac{1}{2}$ hour	ca. 3 hours	$\frac{1}{2}$, 1, 1 $\frac{1}{2}$ and 3 h. after glucose ingestion
0.150—0.200	$\frac{1}{2}$ —1 h.	< 2 h.	?
Av.: 0.130. Var.: 0.024—0.081 above fasting value	$\frac{1}{2}$ h.	ca. 2 h.	5—10 min. in 1' h.; 10—15 min. in 2' h.; then 30—60 min.
Av.: 0.123 Var.: 0.110—0.162	$\frac{1}{2}$ —1 h.	< 3 h.	$\frac{1}{4}$ — $\frac{1}{2}$ — $\frac{3}{4}$ —1—1 $\frac{1}{2}$ 2—3—4 h. after gluc. ingestion
Av.: 0.183 Var.: 0.135—0.242	$\frac{1}{2}$ —1 h.	3 h.	15 min. in 3' h. 30 min. in 4' h.

hours' fasting (with normal fluid intake), and found the blood sugar concentration rising in $\frac{1}{2}$ —1 hour to 4—5 times the initial value, with a very protracted period of hyperglycaemia (more than 3 hours). In tests with reduced supply of water the glucose ingestion gave a blood sugar curve rising to 2—3 times the initial value, but here the hyperglycaemia was even more protracted than in the tests with sufficient supply of water. That this difference was not owing to a marked glycogen shortage in the liver, was demonstrated on subcutaneous injection of adrenalin (2 cc. 1 ‰ sol.), which was followed promptly by a rise of the blood sugar concentration.

So these authors have demonstrated in children, what is also found in adults, that *the carbohydrate tolerance is lowered after protracted fasting.*

Rumpf⁹⁹ has studied the behaviour of the blood sugar in individuals on a *high protein and fat diet*; and he finds that in infants as well as in adults there is a *lowered carbohydrate tolerance* after such a diet, as glucose ingestion is followed by an increased and protracted alimentary hyperglycæmia.

B. OWN INVESTIGATIONS.

Technique and Material.

For my examinations I have used the Hagedorn-Jensen method as it is given in Hagedorn's dissertation⁴², 1921. The principle of the method is that, in alkaline solution under heating, glucose reduces potassium ferricyanide to potassium ferrocyanide. After mixing a known potassium ferricyanide solution with the glucose solution to be estimated, the non-reduced potassium ferricyanide is determined by iodometrical titration, and from this the reducing glucose is calculated. Briefly outlined, the method is carried out as follows:

From a cut in the skin 0.1 cc. of blood is transferred with a capillary pipette into a test tube containing 6 cc. of a precipitant, composed of 1 cc. N/10 sodium hydroxide and 5 cc. of an 0.45 % solution of crystalline zinc sulphate. The tube is placed in water bath for 5 minutes at 100°, whereby the protein is precipitated; after cooling, filtration into a wider test tube, through a small funnel with a little cotton plug. (This cotton has been washed for several hours under running water, so it is free of reducing substances). The first tube is rinsed two times with 3 cc. distilled water, which is also passed through the filter. The filtrate must be clear as water. From an automatic pipette is now added 2 cc. N/200 potassium ferricyanide solution (1.649 gm. potassium ferricyanide — 10.6 gm. calcinated sodium carbonate in distilled water to make 1000 cc.; the solution is kept in a bottle painted black). The mixture is then left standing 15 minutes in boiling water bath for reduction, whereafter it is cooled quickly; then is added 3 cc. of a potassium iodide solution and 2 cc. 3 % acetic acid (the potassium iodide solution consists of 5 gm. iodate-free potassium iodide, 10 gm. crystalline zinc sulphate and 50 gm.

sodium chloride in 200 cc. water). Now titration is made with N/200 sodium thiosulphate solution, with starch for indicator (1 % soluble starch in a saturated solution of sodium chloride). The thiosulphate solution is standardized against a N/200 potassium iodate. The result of the titration is read in a table, taking for entry the amount of thiosulphate solution used in the titration (corresponding to the non-reduced potassium ferricyanide). From the value obtained is subtracted a blind value, blind control analysis being made with every series of blood sugar determinations. The result is given as gram per 100 cc.

To avoid coagulation in the pipette, I have rinsed the pipette between each withdrawal of blood with a 3 % solution of sodium citrate; and this measure has proved most expedient. The citrate solution does not modify the reduction; this has been tried out on venous blood as well as in blind control analyses. In every test the blood was taken and the titration carried out by myself, and every analysis was made on the same day the blood was taken. The precipitation of the protein in the blood samples was done in portions while the samples were being taken, so that the blood was left standing at the most one hour in the precipitant fluid before it was boiled.

The mean error of the method in my hands has been calculated in part from the serial analyses (2—4 blood samples) of the fasting blood sugar, preceding every examination of the blood sugar curve, a total of 725 determinations in 183 serial analyses. On this material the mean error of the method was 0.0023. In addition, I have made 200 analyses on 10 different samples of venous blood. From these results the mean error was computed as 0.0027, that is a little larger than the error above.*) Dr. Hagedorn has told me that the mean error of the method computed from analyses on venous blood is generally a little larger than the mean error on capillary blood. The cause of this difference has not as yet been fully established.

The normal children of this material are divided according to their age into 3 groups. Group I: 11 normal breast-babies, aged 4—14 days. Group II: 20 normal bottle-babies, from 15 days to 11 months and 24 days. Group III: 22 normal children, from 13 months to 13 years and 8 months.

*) The mean error has been computed by A. M. Hemmingsen, Ph. D., Northern Insulin Laboratory.

The normal breast-babies of group I are children born in the lying-in hospital. Group II covers children who have been admitted to this department for very slight ailments (umbilical hernia, mild catarrhs, and for the sake of observation). All these children had been in good health for some time before the blood sugar examination. Group III comprises older children, who had been admitted to the department for various lesions — presumably with no influence upon the carbohydrate metabolism. These children were also clinically normal at the time the blood sugar examination was made. The case-records of Group III will be given in brief abstracts. Finally, the blood sugar regulation has been examined in a number of children suffering from various lesions to be mentioned later.

To all the children examined applies the rule that the living conditions have been as uniform as practicable prior to and during the period when the examination is made — especially with regard to the meals, their composition, number and hours. Particular stress has been laid upon the point that the children did not have any — even very slight — rise of temperature the days before an examination, and also that the bowels have been regular. In the protocols the fasting hours preceding an examination are given in each instance. In group I and II this period has been 5—7 hours, in group III it was 12—15 hours. The examinations was commenced in the morning. The children was brought directly to the examination room — either in their own beds, or in case of the older children on wheel-stretcher — without any break in their resting period. The children have been lying down throughout the examination period. Two children, No. 14 and 21, in group III, who were staying in another department, were allowed to get up and dress and walk to the examination room (2 minutes' walk). Here they were lying down for half an hour before the examinations commenced.

In the infants the blood was taken from the heel, after hyperæmia had been produced with hot water; in the older children the blood has been taken from the lobe of the ear. In all the children the emotional reaction to this procedure has

been very slight. As a rule, the infants have been sleeping the last hour or more out of the 2½ hours the examination has usually taken. The older children have been occupied during the examination with reading or drawing. They have all been feeling well while the examination was going on, but a few have complained a little of tiredness and hunger towards the end of the examination period. In two instances I have noticed faintness and sweating, observations I shall come back to in discussing the hypoglycæmic values.

The glucose was given as a 10 % watery solution, without additions of any kind, of the same temperature as an ordinary warm drink. In a couple of cases where the dose was very large, the glucose was given as a 20 % solution so as to avoid an excessively large amount of fluid. The preparation employed has always been Merck's Glucose puriss. anhydr., and the various supplies have been showing a reduction value calculated as 97—99 % pure glucose. In infants the solution has been given by way of stomach tube, as it was found that it took them too long to drink it. A few times this way of ingestion has been followed by regurgitation; when more than minimal amounts have been brought up, I have discontinued the examination at once. When occasionally some fluid has been left in the tube, it is given afterwards by spoon. The older children have swallowed the glucose solution, always willingly; several have enjoyed the taste of it, and none have objected to it. All the older children have been asked if they were nauseated, and all have denied it. With the exception of one instance, in which the dose was particularly large, there has not been any vomiting in any case, neither in sick nor in well children. Thus I have not experienced the difficulties a few investigators complain of in getting the children to take the glucose solution; possibly this is owing to the purity of the preparation I have used, or it may be because the older children have been made interested in the examination, or they have taken the sugar solution as a reward for good behaviour while the fasting blood samples were taken. None of the

children — infants or older ones — have had any intestinal disturbances in connection with the examination.

Prior to each tolerance test, 3—4 samples of fasting blood have been taken in immediate succession. The fasting value recorded is the average result of these determinations. The time it has taken to give the child the solution — either by way of stomach tube or by the child's drinking it — is recorded in every instance in the protocols. It has been a matter of only a few minutes. A sample of the blood is taken immediately after the glucose ingestion, and from now on blood is taken at intervals of 5 minutes through the first hour and a half, and at intervals of 10 minutes in the next hour, the average examination period being $2\frac{1}{2}$ hours.

In the first series of tests, double samples of blood were taken every 10 minutes, and the interval between the two samples of each set was usually $1\frac{1}{2}$ —2 minutes. It was soon found, however, that during the rise of the blood sugar concentration the difference between the values of the two samples in each set was greater than the mean error of the method in so many instances as to indicate a real difference in the glucose content of the two samples; and consequently it gave a false picture of the blood sugar rise when the calculated mean values of each pair of samples were used for construction of the blood sugar curve. So I turned to the above-mentioned plan of taking blood samples. When the analyses are made in duplicate, both values are entered in the protocols. When parallel tests are made on the same individual, several days have passed between the tests, leaving out any chance of effect from a preceding ingestion of glucose.

In describing the curves, I use the term maximal value as designating the highest point in the hyperglycaemic curve. By the term »rise« I mean the difference between the maximal blood sugar value and the fasting value. For practical reasons, in the description, I take the hyperglycaemia as passed when, after its first rise, the blood sugar concentration has returned to a level of 0.100 % or less, though I am well aware that occasional secondary rises are also to be included in the course

of the alimentary blood sugar curve. By hypoglycæmia I mean blood sugar values less than 0.070 %.

In the graphs of the blood sugar curves (see, for inst., Fig. 12, p. 46), the cipher 0 designates the first blood sample after ingestion of glucose. The preceding value — the first value entered — designates the fasting value. The distance between these two values indicates the time occupied with the procedure of glucose ingestion — naturally it is subject to some variation — plus one minute, the time gone with taking the first blood sample after completion of the glucose ingestion.

With this technique I have aimed in particular to ascertain whether children are subject to greater lability than are adults with regard to the blood sugar concentration, or if, on the contrary, repeated tolerance tests may give more uniform blood sugar curves in children than in adults. For it is much more easy to keep children, especially infants, under uniform outer conditions and thus, at least to a large extent, leave out any varying exogenous factors.

1. Blood Sugar in Fasting Children.

I shall first mention the fasting blood sugar values I found in connection with the subsequent glucose tolerance tests on three groups of children:

Group I comprises 11 new-born children, aged 4—14 days, with a total of 22 examinations. Fasting period 5—5½ hours. Here the average fasting value is 0.083 %, in variations from 0.066 to 0.099 %.

Group II: 20 infants, from 15 days to 1 year old, with a total of 46 examinations. Fasting period 6—6½ hours. The average fasting value is 0.080 %, in variations from 0.067 to 0.101 %.

To the same age-class belong some children in whom the tolerance tests were made with saccharose as well as with

glucose — 6 children, aged 1—8 months, with a total of 12 examinations. Fasting period 6—6½ hours. In these children, too, the average fasting value is 0.080 %, while the variations range from 0.062 to 0.089 %.

Group III: 22 children, aged 1—13 years, with a total of 43 examinations. Fasting period 14—15 hours. Here the average fasting value is 0.088 %, in variations from 0.068 to 0.099 %.

So, in the first two weeks of life as well as in the whole first year of life there appears to be a tendency to fasting values somewhat lower than those encountered in adults, whereas the fasting values in older children are practically the same as the values usually observed in normal adults.

In 11 children, varying in age from 2 months to 7 years, a total of 14 serial examinations of the fasting blood sugar concentration were made after a fasting period of 3½—15 hours. The examination period was 2—3½ hours, during which the children kept on fasting. Blood samples were taken every 10 or 15 minutes. In some instances, double samples of the blood were taken; in such cases, both values are recorded in the protocols. Table 5 p. 44) gives the average fasting values obtained in these serial examinations and, in each instance, the maximal deviations from the respective average.

In most of the cases the variations were small, and many of them fall within the limits of the mean error of the method. In most of these cases, however, the blood sugar curve shows some low, rather long, waves, lasting ½ hour or more (cf., for inst., Fig. 1, 2, 3 and 4). But, one case forms a striking exception to this rule. This was the case of a perfectly healthy child, 2½ months old, who at the beginning of the examination

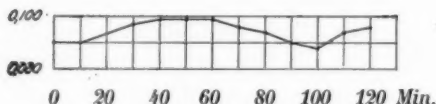


Fig. 1.

No. 4. Female, 6½ months. Preceding fasting period 6½ hours.

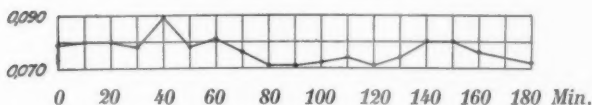


Fig. 2.

No. 6. Male, 8½ months. Preceding period 6 hours.

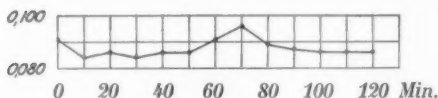


Fig. 3.

No. 7. Male, 11¾ months. Preceding fasting period 6½ hours.

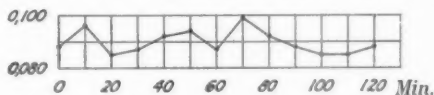


Fig. 4.

No. 8. Male, 3¼ months. Preceding fasting period 6½ hours.

had been fasting 3½ hours after an ordinary meal, consisting of 2 parts of milk and 1 part of barley water with 2 % cane sugar. At the beginning of the examination, the blood sugar was 0.067 %, and within the next 30 minutes it rose gradually to 0.091 %; then it stayed at this level the next 40 minutes, whereafter there was a sudden rise to 0.138 %. From this, the blood sugar concentration fell off gradually during the next ½ hour, in which 5 samples were taken, till it was again 0.091 %. In the next hour there were but a few small variations (Fig. 5). No demonstrable cause of this paradoxal rise of the blood sugar could be made out. The child was feeling well, did not react particularly vigorously on the blood-taking, had no rise of temperature, and presented no other abnormality whatever. One might think that this was a question of alimentary influence from the meal taken 4½ hours before; but this does not seem very likely. Perhaps it would be more reasonable to associate such a variation with emotional excitement; but, as already mentioned, there was no evidence of

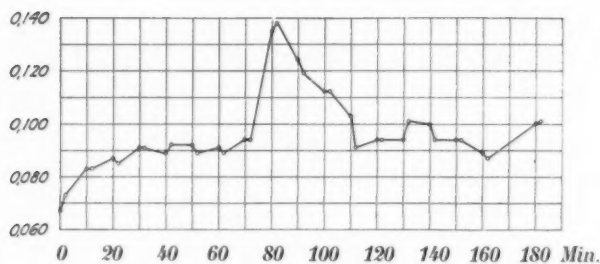


Fig. 5.

No. 1. Female, 2½ months. Preceding fasting period 3½ hours.

any such emotional condition, and, if so, the sudden rise would also have been more apt to come in the beginning of the examination and not an hour later. A new examination performed under exactly the same conditions 4 days later did not bring out any variations whatever from the findings obtained in other children (Fig. 6).

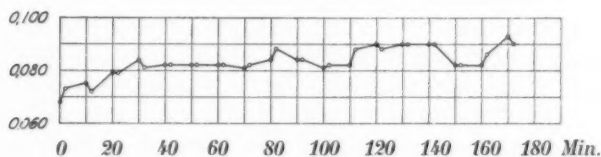


Fig. 6.

No. 1. Female, 2½ months. Preceding fasting period 3½ hours.

In one case (Fig. 7) there was a difference of 0.022 % between two samples of blood taken 10 minutes apart, which in this case means 0.013 % below and 0.009 % above the

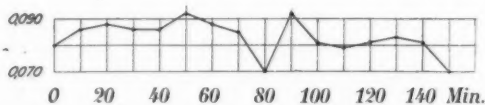


Fig. 7.

No. 3. Male, 4 months. Preceding fasting period 3½ hours.

average fasting value. This was the greatest difference observed between any two consecutive samples. In cases where the blood sugar determinations were made in duplicate, their variations did not exceed the error of the method. As will be noticed, in some cases — e. g., No. 2, 5 and 6 (Fig. 8, 9 and 10, 11) — the blood sugar concentration stayed at quite the same level through half an hour or more.

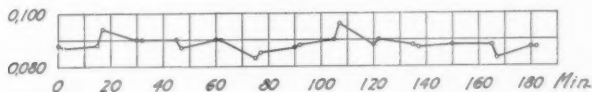


Fig. 8.

No. 2. Male, $3\frac{1}{2}$ months. Preceding fasting period $3\frac{1}{2}$ hours.

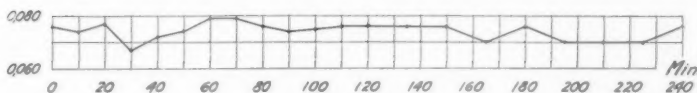


Fig. 9.

No. 5. Female, $6\frac{3}{4}$ months. Preceding fasting period $3\frac{1}{2}$ hours.

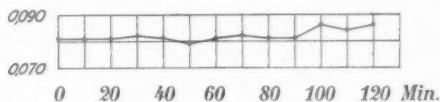


Fig. 10.

No. 6. Male, $8\frac{1}{2}$ months. Preceding fasting period 4 hours.

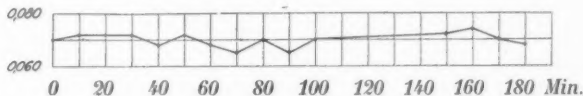


Fig. 11.

No. 3. Male, 4 months. Preceding fasting period $3\frac{1}{2}$ hours.

In these examinations, as already mentioned, the individuals have been fasting $3\frac{1}{4}$ —15 hours before the examination commenced. There has been good agreement between the values obtained after the different fasting periods.

Leaving out the variations that may be due to errors of the method, one has the impression, 1) that *the fasting blood sugar concentration is subject to variations which do not as a rule take the form of abrupt oscillations but run a smooth and long-drawn, undulating course, during which the blood sugar concentration keeps within the usual limits for fasting values in normal individuals; and*

2) *the variations in the fasting value from day to day in the same individual will largely depend upon the level of this fasting curve — apex or bottom — at the time the blood is taken.* The one case in which I found an abnormally high rise of the blood sugar — in such a way that a technical error is absolutely out of the question as an explanation — may perhaps throw some light on those cases described by other authors now and then, where an apparently normal individual shows occasionally an abnormally high concentration of the fasting blood sugar. On such an occasion the blood sample may have been taken exactly at the top of such an infrequent high wave.

Table 5.
Fasting Blood Sugar Values in Normal Children.

Case No.	Age	Average o/o	Maximal Variations o/o	Greatest Deviations from the Average	
				Mgm. o/o	
1.	2 months	0.096	0.067—0.133	÷ 29	+ 42
»	»	0.083	0.068—0.093	÷ 15	+ 10
2.	3 »	0.089	0.083—0.096	÷ 6	+ 7
3.	4 »	0.083	0.070—0.092	÷ 13	+ 9
»	»	0.070	0.065—0.074	÷ 5	+ 4
4.	6 »	0.094	0.088—0.099	÷ 6	+ 5
5.	6 »	0.074	0.067—0.079	÷ 7	+ 5
6.	8 »	0.082	0.079—0.086	÷ 3	+ 4
»	»	0.077	0.071—0.089	÷ 6	+ 12
7.	11 »	0.088	0.084—0.096	÷ 4	+ 8
8.	3 years	0.090	0.085—0.099	÷ 5	+ 9
9.	3 »	0.099	0.091—0.105	÷ 8	+ 6
10.	4 »	0.092	0.087—0.101	÷ 5	+ 9
11.	7 »	0.095	0.088—0.101	÷ 7	+ 6

2. Blood Sugar after Glucose Ingestion.

a. Group I. New-born.

(Age, 4—14 Days).

Uniform Tolerance Test.

The children of this group, as mentioned before, are healthy breast-babies, with a normal weight at birth and born at full term, excepting one case (No. 11) where the child was premature by 3 weeks. All the children were examined twice during their first 2 weeks of life, at an interval of 5—9 days. Each examination covered 2½ hours, and the children were examined fasting, 5—5½ hours after the last meal. The glucose was given in a dosage of 2 grams per kilogram of body weight, in form of a 10 % watery solution. This dose was decided on as the standard dose for a glucose tolerance test on infants, because the amount of glucose ingested is not all too small, and the amount of solvent fluid is so large that the amount adherent to the tube and the funnel employed for the ingestion is relatively insignificant.

In describing the blood sugar curves found in these children after the glucose ingestion I shall mention separately the findings in the premature child.

In the first of these children (No. 1) the first glucose tolerance test was made when the child was 8 days old. Here the rise of the blood sugar concentration was very slow and very slight, giving a very low and elongated curve. The maximal value was only 0.014 % above the fasting value, and it was not reached until 65 minutes after the glucose ingestion. After 2½ hours, when the examination was discontinued, the blood sugar value was 0.078 % (fasting value 0.068 %). Thus we have here a pronounced »level curve«, and the hyperglycæmia is so slight that it does not exceed the limit of the fasting values. The next tolerance test, given 5 days later under exactly the same conditions, showed a gradual rise of the blood sugar concentration to 0.176 % in 70 minutes, followed

by a rather sudden fall, the initial value being reached in 120 minutes. The blood sugar concentration was falling off further, and at the conclusion of the test — $2\frac{1}{2}$ hours after the glucose ingestion — it had fallen to a hypoglycaemic value of 0.048 %. Here, then, we meet with an extraordinarily marked difference between the two curves: a difference between the maximal values of the two curves amounting to 0.094 %, and an equally conspicuous difference in the configuration of the hyperglycaemic curves (Fig. 12).

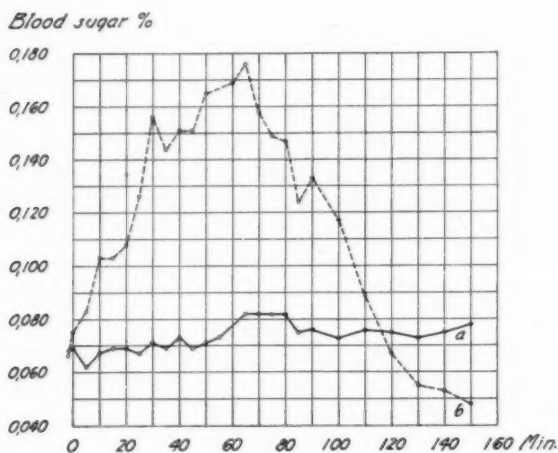


Fig. 12.

Group I, No. 1. Male — a, 8 days. 2 gm. glucose per kg.
 b, 13 " " " " " "

Further examinations of the blood sugar rise after glucose ingestion in the first and second weeks of life showed that this finding was hardly attributable to a mere accident. The maximal values obtained in the first week of life were averaging 0.132 %, with variations from 0.082 to 0.159 %. These maximal values were reached in 25—70 minutes, on an average 50 minutes, and the hyperglycaemia was usually at an end in less than 2 hours. As to the form of the blood sugar curves, various

types are represented even in the first week of life: as will be seen from the figures 12—19 inclusive.

After the conclusion of the alimentary hyperglycæmia, 3 cases (No. 4, 6, 9) showed hypoglycæmic values respectively 130, 140 and 130 minutes after the glucose ingestion (the minimal blood sugar value was respectively 0.039, 0.063 and 0.067 %). At the conclusion of the examination all of these 3 curves showed a tendency to rise anew. In the other cases the blood sugar values at the end of the examination were more or less at the level of the fasting blood sugar values.

In the second week of life all the cases showed maximal values above 0.140 %, averaging 0.165 %, with variations from 0.143 to 0.197 %. The rise of the blood sugar concentration was completed in 20—60 minutes; and in all the cases the blood sugar curve came down to the level of the fasting values within 2½ hours after the glucose ingestion. After the return to the initial level, 3 curves showed a little after-rise (No. 4, Fig. 14; No. 7; and No. 9, Fig. 17). In 3 cases (No. 1, 3 and 5) the blood sugar curves fell off to hypoglycæmic values (0.048, 0.064, and 0.067 %). In No. 1 the hypoglycæmic values were found at the end of the examination, in No. 3 and 5 they were reached 120 minutes after the glucose ingestion, and in these 2 cases there was a tendency to an after-rise at the end of the examination.

The difference between the height of the blood sugar curves in the two examinations — in first and second weeks of life — is so pronounced that the average of the maximal values on the first examination is 0.132 %, and on the second examination 0.165 %, which corresponds with an average blood sugar rise in the two tests of 0.047 and 0.082 %, respectively. *So there can hardly be any doubt that in the new-born there is actually a real difference in the blood sugar rise after glucose ingestion in the first and second weeks of life. For, even though the material is not very large, the mentioned peculiarity is still so constant in its occurrence that it can hardly be a matter of an accidental finding.*

Only No. 5 did not show any difference between the maximal values on the two examinations.

I have looked into whether this peculiar difference of the blood sugar curve in the glucose tolerance test in the first and second weeks of life might be somehow connected with the thriving of the child. Table 6 gives the weight of the respective children at the time of the two examinations.

Table 6.

Case No.	1. examination	2. examination
	Difference in weight since birth	Difference in weight since 1' exam.
	Grams	Grams
1.....	+ 150	+ 270
2.....	+ 200	+ 80
3.....	÷ 100	+ 50
4.....	0	0
5.....	÷ 150	+ 100
6.....	+ 50	+ 200
7.....	0	+ 100
8.....	+ 50	+ 50
9.....	0	÷ 50
10.....	÷ 50	+ 220
11.....	+ 100	+ 100

From this tabulation it is evident that there does not seem to be any connection between the increase or decrease of the body weight and the appearance of the blood sugar curve; in the two series of examinations, large differences between the two blood sugar curves are found in cases with a rather marked gain in weight (as in No. 1) as well as in cases where the weight increase is only slight (e. g., No. 7), and even in cases where there is a loss of weight (as in No. 9) or no change in the weight (e. g., No. 4).

For the sake of comparison, Table 7 gives the average maximal value and the average blood sugar rise in glucose tolerance tests on the first and second examinations of newborn, infants, and older children.

Table 7.
Average Maximal Value and Blood Sugar Rise after Ingestion
of 2 gm. Glucose per kg.

Group of Children	Average Maximal Value			Average Blood Sugar Rise		
	I. 1-14 days	II. 15 d-1 year	III. 1-13 years	I.	II.	III.
1' exam. ...	0.132	0.170	0.157	0.047	0.088	0.067
2' exam. ...	0.165	0.175	0.154	0.082	0.094	0.066

This table shows that there is a very conspicuous difference in the maximal values of the blood sugar concentration on the first and second examinations in the new-born, whereas the other two groups show no such difference. So these examinations have established the fact that *the hyperglycæmia produced by glucose ingestion (2 gm. per kg. in 10 % solution) in the first week of life is on an average considerably lower than the hyperglycæmia produced under the same conditions in the second week of life or later in infancy.*

It may further be pointed out that even as early as in the second week of life the average maximal blood sugar value approaches the values usually obtained under the same conditions later in infancy (Group II), which are considerably higher than the average maximal values in older children (Group III) — a finding I shall later come back to.

As to the premature child, both tolerance tests (in 1. and 2. week of life) give very low and elongated blood sugar curves. But here the blood sugar rise is highest in the first test — namely, 0.039 % — with a maximal value of 0.114 %. The second test shows a rise of 0.025 %, with a maximal value of 0.096 %. In the first test the hyperglycæmia reaches its maximum in 35 minutes and is then staying on this plateau for about half an hour, whereafter it takes a rather abrupt fall to fasting level, and then again a little after-rise in the last half

hour. This fall and subsequent after-rise are not found on the second test (see Fig. 19). This difference in the two tests is insignificant, however; the main features of both the curves are the slight rise of the blood sugar and their pronounced plateau type.

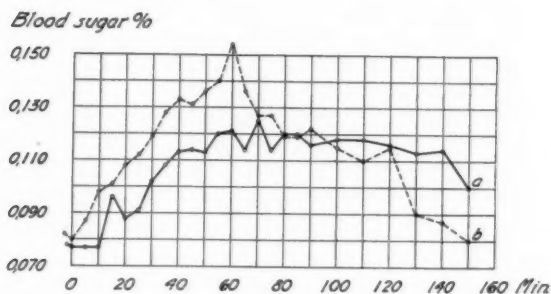


Fig. 13.

Group I, No. 2. Male — a, 8 days. 2 gm. glucose per kg.
b, 13 " " " " " " "

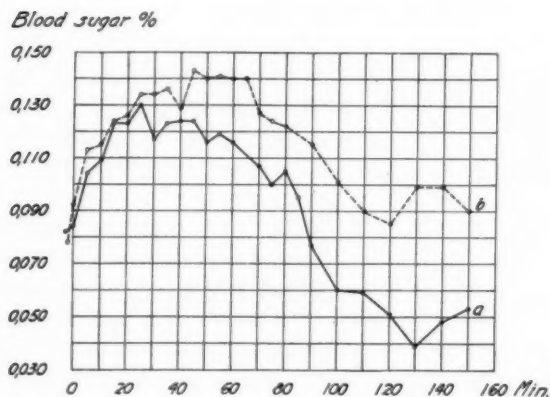


Fig. 14.

Group I, No. 4. Male — a, 7 days. 2 gm. glucose per kg.
13 " " " " " " "

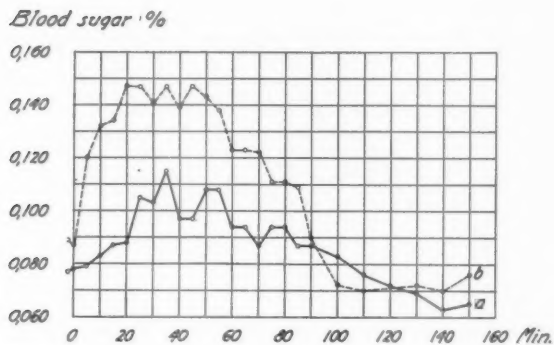


Fig. 15.

Group I, No. 6. Male — a, 5 days. 2 gm. glucose per kg.
b, 14 » » » » » » »

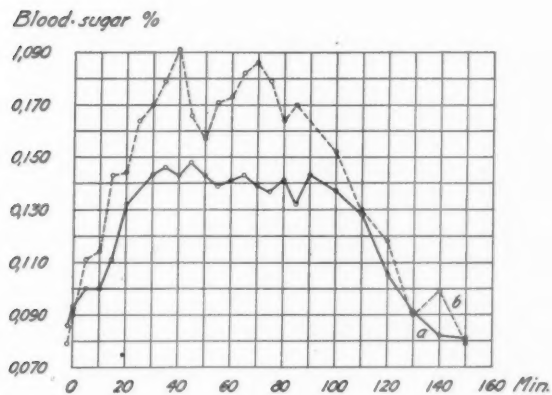


Fig. 16.

Group I, No. 8. Female — a, 7 days. 2 gm. glucose per kg.
b, 12 » » » » » » »

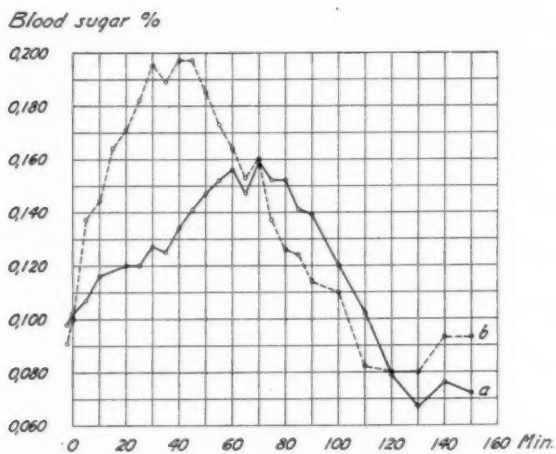


Fig. 17.

Group I, No. 9. Female — a, 7 days. 2 gm. glucose per kg.
 b, 14 » » » » » » » »

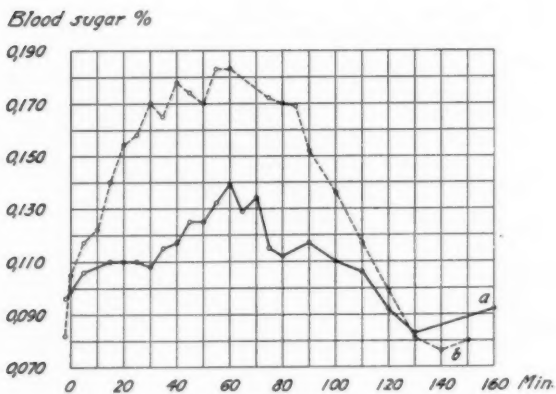


Fig. 18.

Group I, No. 10. Male — a, 7 days. 2 gm. glucose per kg.
 b, 12 » » » » » » » »

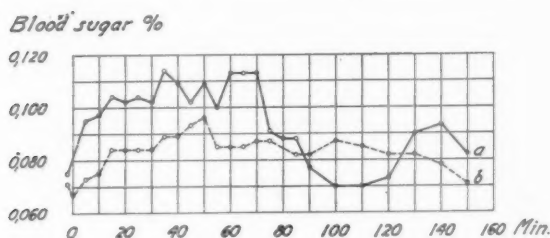


Fig. 19.

Group I, No. 11. Male — a, 7 days. 2 gm. glucose per kg.

b, 12 " " " " " "

Table 8 gives the most important data on the course of the alimentary hyperglycæmia in these tolerance tests on newborn. It will be noticed that *while the two parallel tests show a considerable difference in the alimentary hyperglycæmia, there is no difference in the average fasting value* (respectively 0.084 and 0.083 %).

Table 8.

a. Alimentary Hyperglycæmia after Glucose Ingestion (2 gm. per kg.) in 1. and 2. Week of Life. 11 Children.

	1' Examination Age: 4—8 days		2' Examination Age: 11—14 days	
	Average	Variations	Average	Variations
Fasting values %.....	0.084	0.068—0.098	0.083	0.066—0.099
Maximal values %.....	0.132	0.082—0.159	0.165	0.096—0.197
Rise of blood sugar %.	0.047	0.014—0.064	0.082	0.025—0.112
Time for max. val. in minutes after gluc. ingest.	50	25—70	50	20—65
Duration of hyperglycæmia in min.	105	60—150	112	90—130

b. Individual Differences of the Values in the two parallel Tests.

Differences in	Average	Variations
Fasting values %/0.....	0.006	0.002—0.014
Maximal values %/0.....	0.031	0.001—0.094
Rise of blood sugar %/0..	0.033	0.001—0.096
Time for max. val. after gluc. ingest. in min....	14	0—30
Duration of hyperglycæ- mia in min.....	14	0—55

*b. Group II. Infants.**(Age, 15 days—1 year).**Uniform Tolerance Tests.*

This group comprises 20 children under one year. All these children had been admitted to the department for very mild ailments, and they have all been perfectly well for several weeks or months before their blood sugar regulation was examined. As a rule, the parallel tests on each individual were made at an interval of 4—7 days; in 2 cases the interval was 2 days, and in 2 cases it was respectively 27 and 34 days. During the examination period the diet was not changed in any of the cases, except in No. 2 (interval of 27 days) where the milk mixture was modified. The children had all been fasting 6—6½ hours before each examination. In each test the dose of glucose was 2 grams per kilogram of body weight, given — as a 10 % solution — through stomach tube. No. 4 and 17 were examined but once.

In these examinations the average fasting value was

0.080 %, with variations ranging from 0.067 to 0.101 %. The average difference of the fasting values on examination of the same individual on two different days was 0.010 %, and the greatest difference in the same individual was 0.022 %; in some cases there was no difference.

The average maximal value after glucose ingestion was 0.172 %; the lowest maximal value was 0.109 %, the highest 0.250 %. In some instances the maximal value was reached as early as 10—25 minutes after the glucose ingestion; and, on the other hand, in a few instances it took 60—70 minutes to reach the maximum. On an average the maximal value was obtained 35 minutes after the glucose ingestion.

In half of the tests the maximal values were over 0.180 %, in 8 instances they were over 0.200 %, and in 5 of these they were from 0.220 to 0.250 %. So, unquestionably, the maximal values I have obtained in infants are far greater than the maximal values usually observed in adults, and — as I shall show later — they are also much higher than the maximal values generally obtained in older children.

The duration of the hyperglycaemia was on an average 85 minutes. In one instance it lasted but half an hour (No. 14₁,*) Fig. 26). On the other hand, in two instances the blood sugar curve had hardly returned to the fasting level when the examination was discontinued (No. 8₁, Fig. 22; No. 12₁, Fig. 24).

The appearance of the blood sugar curves was subject to a great deal of variation. Thus there are curves with a rather gradual rise, with maximal values under 0.160 %, keeping at the level of the maximal value — with minor variations — for ½ hour or more, and with the subsequent fall more or less gradual (No. 1₁, Fig. 20; No. 2₁, Fig. 21; No. 8₂, Fig. 22); Other curves show a gradual but rather high rise, to maximal values about 0.180 % or more (No. 8₁, Fig. 22; No. 10_{1,2}, Fig. 32; No. 18₂, Fig. 27); and some curves display an abrupt — in some instances very high (above 0.200 %) — rise and an

*) The lower ciphers — 1 and 2 — designate respectively the first and the second of the parallel tests; 1,2 means both tests.

abrupt fall, so that the hyperglycæmia is over in 1—1½ hour (No. 2, Fig. 21; No. 7_{1,2}, Fig. 30; No. 11, Fig. 23; No. 14, Fig. 26; No. 18, Fig. 27).

Hypoglycæmic values were found on both tests in 7 children (No. 6, 7, 9, 11, 13, 15) and on one of the tests in 4 children (No. 5, 10, 16, 19). The hypoglycæmic values were varying from 0.005 to 0.046 % below the respective fasting values, on an average 0.023 % below. The lowest absolute value was 0.038 %. As a rule, the hypoglycæmia appeared about 2 hours after the glucose ingestion, but occasionally it came on even in ca. 1 hour (No. 6 and 7). In the last two cases the hypoglycæmia was followed in 20—40 minutes by an after-rise — amounting respectively to 0.028 and 0.039 % — which again was followed by a new period of hypoglycæmia (Fig. 30). There were not observed any clinical signs of a hypoglycæmic reaction in any of these infants, but as most of them were sound asleep throughout the last hour of the examination period, it is not absolutely excluded that some slight hypoglycæmic symptoms may have been present without being noticed.

In contrast with Herlitz, then, I have to maintain that *a fall of the blood sugar concentration to hypoglycæmic values after an alimentary hyperglycæmia (from glucose ingestion) is a common finding in infants* when the examination covers a period of 2½ hours.

After-rise of the blood sugar curve before hypoglycæmic values had been reached was observed in No. 2, 3, 4, 8, 10, 12, 14, 17, 18, and 20.

As already mentioned, these children have all been fasting 6—6½ hours before each examination. For infants such a period forms a natural night-pause after the evening meal (usually consisting in a milk mixture), and that is why I decided on a fasting period of this length. This fasting period is only about half as long as the natural fasting period in adults usually employed in tolerance tests on these (12—14 hours), and it may possibly be that this has something to do with the greater rise of the alimentary hyperglycæmia in

these children. In this connection it may be mentioned that Staub (108) finds the greatest blood sugar rise from glucose ingestion about 5 hours after a meal, while K. M. Hansen finds the greatest rise in such tests 4 hours after a meal. But, the last two fasting periods are 1—2½ hours shorter than the fasting period employed in my examinations.

Herlitz⁵⁰ and Rumpf⁹⁹ have made investigations with a technique rather similar to the one I have been using, but their dose of glucose was only 1.3 gram per kilogram of body weight, and their maximal values are not near as high as my findings. Thus, Herlitz gives 0.162 % as the highest absolute value, and Rumpf finds 0.081 % as the highest rise above the fasting value, whereas I find an *average* rise of 0.091 % above the fasting value and a maximal rise of 0.165 %. Herlitz employed a fasting period of 5 hours, and Rumpf used a fasting period of 13 hours in the test that gave the value mentioned above. The difference between the results of these two authors and my own findings is explainable most correctly, I think, by the facts that I have been taking the blood samples at shorter intervals so I have been less liable in some instances to miss the higher values, and also that I have employed a larger dose of glucose.

There is a very marked difference in the results of the parallel examinations on different days in this group of children. But, as mentioned before (p. 49), one does not here — as in the new-born — find any regular difference in the hyperglycæmic values of the first and second tests, the hyperglycæmia being sometimes greater and sometimes less on the first test than on the next. In this group of children the difference in the rise of the blood sugar in two parallel tests is on an average 0.031 %. In a few cases the difference is but very slight (e. g., 0.002 %); in one case it is as great as 0.105 % (Fig. 25). As a contrast to this, it may be mentioned that similar parallel tests on older children show an average difference of 0.010 % and a maximal difference of only 0.022 % (cf. Group III, p. 68); and for the sake of comparison I may again quote the investigations of Hagedorn⁵⁰ and

Soisalo¹⁰⁶. In adults, these authors find respectively 0.047 and 0.052 % as the greatest difference between two parallel tests on the same person under identical conditions, but as a rule they find the difference considerably smaller.

Also the appearance of the hyperglycæmic curve is subject to marked differences in these parallel tests, as illustrated in No. 1, 2, 8, 11, 12, 13, 14, 18, 19, 20 (Fig. 20—29 inclusive).

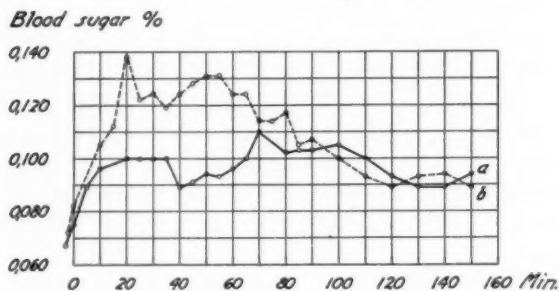


Fig. 20.

Group II. No. 1. Female. a, 15 days. 2 gm. glucose per kg.
b, 20 » » » » » » »

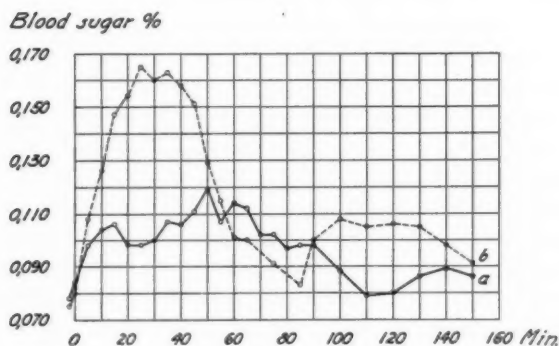


Fig. 21.

Group II. No. 2. Male. a, 17 days. 2 gm. glucose per kg.
b, 44 » » » » » » »

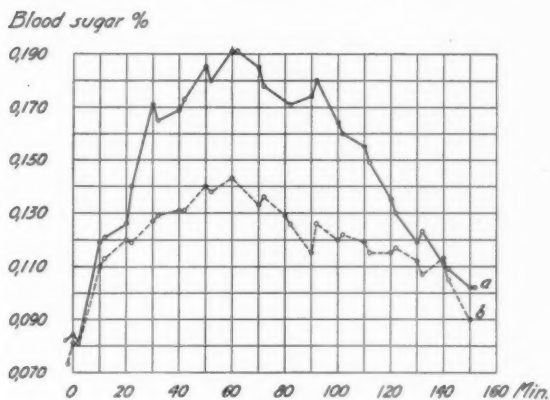


Fig. 22.

Group II. No. 8. Male. a, 3 mths. 5 days. 2 gm. gluc. per kg.
b, 3 " 9 " " " " " " " " " " " "

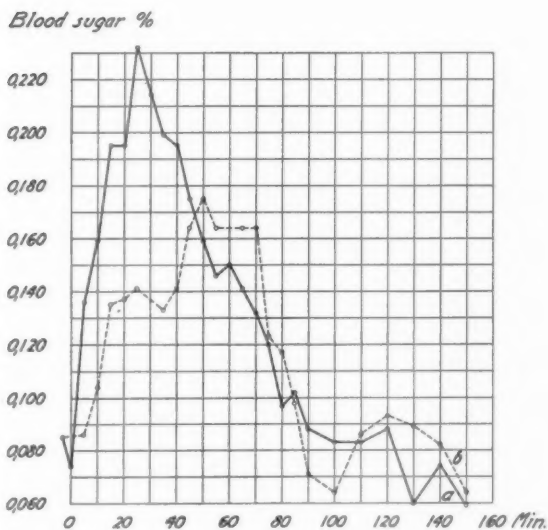


Fig. 23.

Group II. No. 11. Female. a, 3 mths. 17 d. 2 gm. gluc. per kg.
b, 3 " 21 " " " " " " " " " " " "

Blood sugar %

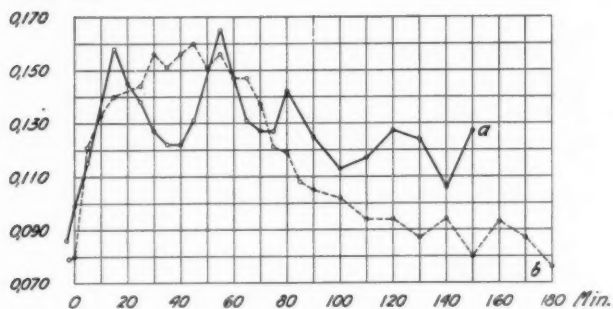


Fig. 24.

Group II. No. 12. Male. a, 4 mths. 8 d. 2 gm. gluc. per kg.

b, 4 » 12 » » » » » » »

Blood sugar %

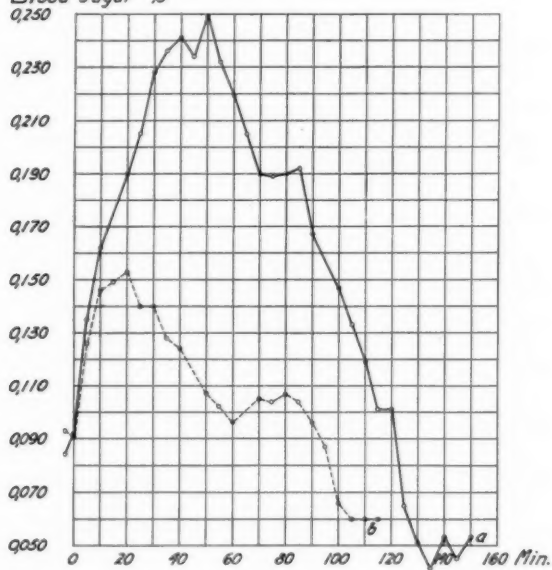


Fig. 25.

Group II. No. 13. Male. a, 5 mths. 24 d. 2 gm. gluc. per kg.

b, 5 » 28 » » » » » » »

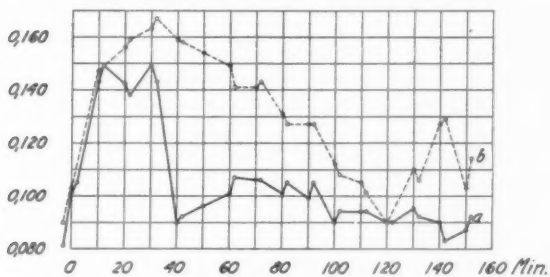
Blood sugar %

Fig. 26.

Group II. No. 14. Male. a, 6 mths. 23 d. 2 gm. gluc. per kg.

b, 6 » 27 » » » » » » »

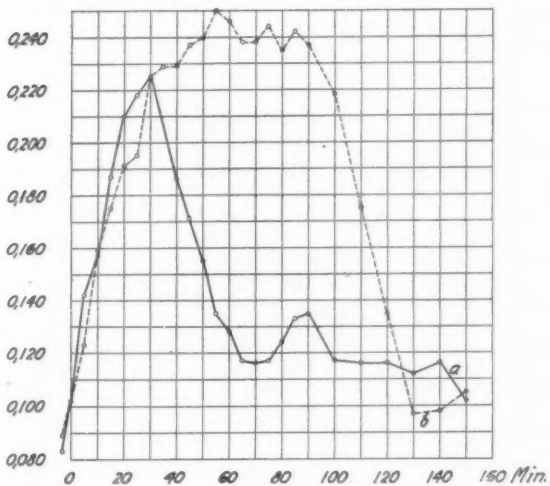
Blood sugar %

Fig. 27.

Group II. No. 18. Male. a, 9 mths. 22 d. 2 gm. gluc. per kg.

b, 9 » 28 » » » » » » »

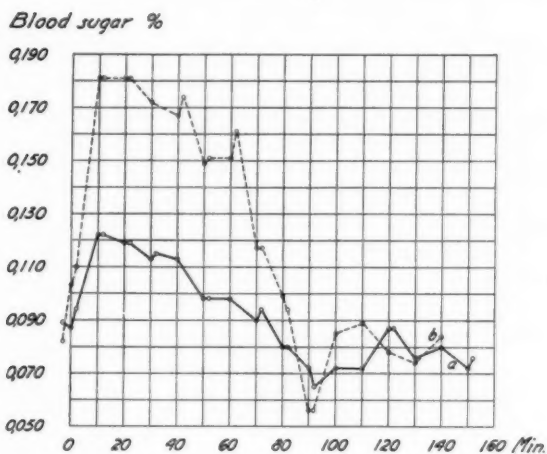


Fig. 28.

Group II. No. 19. Male. a, 11 mths. 22 d. 2 gm. gluc. per kg.
b, 12 » 12 » » » » » » »

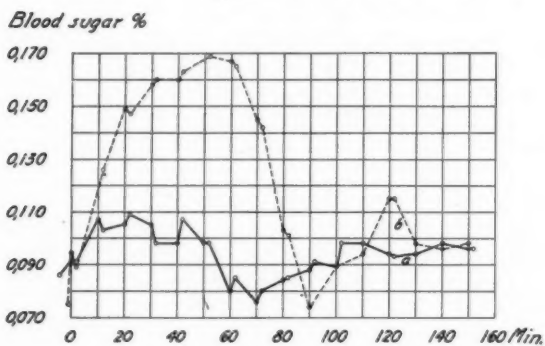


Fig. 29.

Group II. No. 20. Male. a, 11 mths. 24 d. 2 gm. gluc. per kg.
b, 12 » 13 » » » » » » »

On the other hand, the curve may also be of the same type in both tests, as shown in No. 3, 6, 7 (Fig. 30), 9, (Fig. 31), 10, (Fig. 32), 15, (Fig. 33), 16, (Fig. 34). In No. 7 (Fig. 30) and No. 9 (Fig. 31) the curves are almost identical — within the

limits of experimental error — with regard to the primary rise and fall. Both curves have after-rises, but at different times.

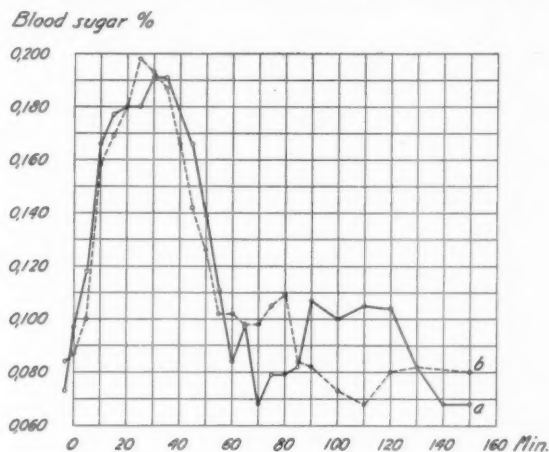


Fig. 30.

Group II. No. 7. Female. a, 3 mths. 26 d. 2 gm. gluc. per kg.
b, 3 " 28 " " " " " "

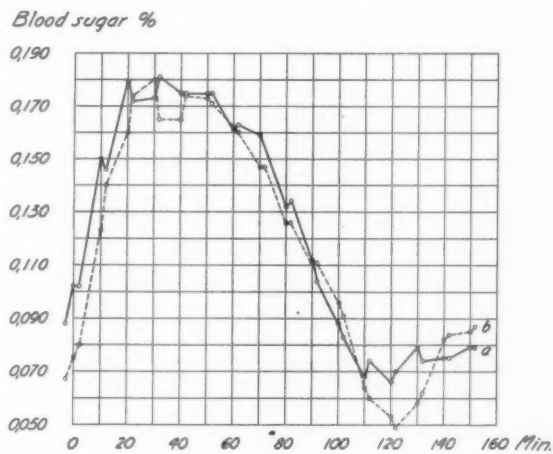


Fig. 31.

Group II. No. 9. Male. a, 3 mths. 5 d. 2 gm. gluc. per kg.
b, 3 » 12 » » » » » »

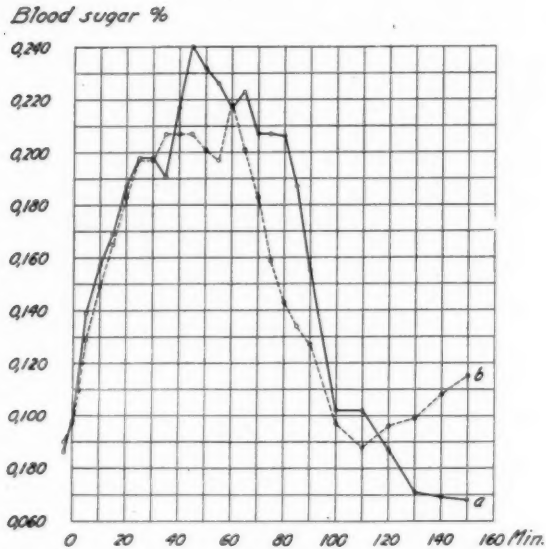


Fig. 32.

Group II. No. 10. Male. a, 3 mths. 16 d. 2 gm. gluc. per kg.
 b, 3 » 22 » » » » » » » »

In most of these cases there is also a marked difference in the duration of the hyperglycemia in the parallel tests, even up to 80 minutes. On an average, this difference is 30 minutes.

As to the cases with marked individual differences of the curves in the parallel tests, the differences of maximal value and blood sugar rise in each of these have been tabulated in Table 9, (p. 66).

In No. 12 the difference of the curves is not so much in the maximal values obtained, it being only 0.005 %, as in the configuration of the curves (see Fig. 24).

There is no relation between the changes in the weight of the children and the appearance of the curves (Table 10, p. 66).

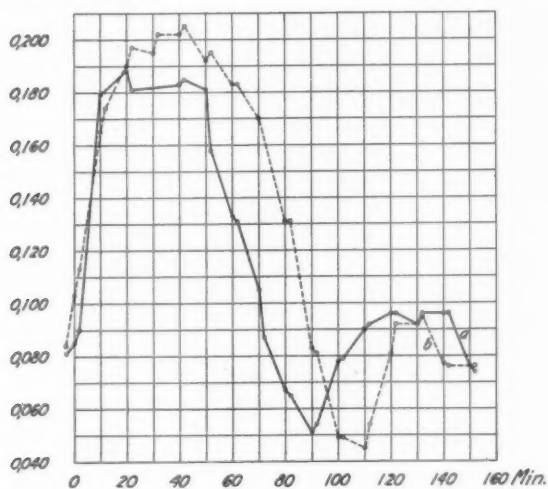
Blood sugar %

Fig. 33.

Group II. No. 15. Male. a, 9 mths. 3 d. 2 gm. gluc. per kg.

b, 9 " 7 " " " " " " "

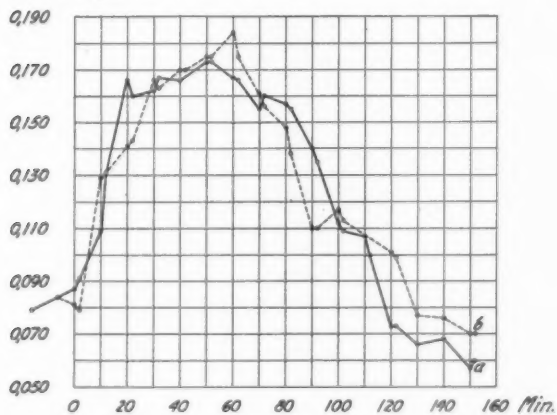
Blood sugar %

Fig. 34.

Group II. No. 16. Male. a, 9 mths. 8 d. 2 gm. gluc. per kg.

b, 9 " 11 " " " " " " "

Table 9.
Individual Differences of the Blood Sugar Curves in Parallel Glucose Tolerance Tests.

No.	1. Difference in maximal value 0.038 %, in rise of curves 0.033 %											
»	2.	»	»	»	»	0.046	»	»	»	»	0.049	»
»	8.	»	»	»	»	0.048	»	»	»	»	0.039	»
»	11.	»	»	»	»	0.047	»	»	»	»	0.047	»
»	13.	»	»	»	»	0.096	»	»	»	»	0.105	»
»	14.	»	»	»	»	0.018	»	»	»	»	0.019	»
»	18.	»	»	»	»	0.025	»	»	»	»	0.019	»
»	19.	»	»	»	»	0.059	»	»	»	»	0.066	»
»	20.	»	»	»	»	0.060	»	»	»	»	0.071	»

Table 10.
Differences in Weight at Time of Parallel Tests.

No.	1' examination	2' examination
1.....	Weight: 3410 gm.	÷ 10 gm.
» 2.....	» 3350 »	+ 490 »
» 3.....	» 4940 »	+ 130 »
» 5.....	» 4310 »	+ 15 »
» 6.....	» 3550 »	+ 125 »
» 7.....	» 4240 »	0 »
» 8.....	» 5770 »	+ 210 »
» 9.....	» 4870 »	+ 130 »
» 10.....	» 5050 »	+ 180 »
» 11.....	» 4280 »	+ 95 »
» 12.....	» 7150 »	÷ 120 »
» 13.....	» 5940 »	+ 60 »
» 14.....	» 8000 »	+ 200 »
» 15.....	» 7960 »	+ 260 »
» 16.....	» 8800 »	÷ 100 »
» 18.....	» 7700 »	+ 730 »
» 19.....	» 9230 »	+ 70 »
» 20.....	» 6600 »	+ 400 »

So there can be no doubt that children under one year are much more subject to individual variations in alimentary hyperglycæmia than are older children and adults, although the diet and other living conditions of these infants are as uniform from day to day as possible.

Bekendtgørelse.

I Henhold til kgl. Anordning af 13. Oktober 1927 er der fastsat følgende Bestemmelser til Ordens Opretholdelse ved det offentlige Forsvar af Doktorafhandlinger:

1. Forsvarshandlingen ledes af Fakultetets Dekanus eller af en anden dertil af Fakultetet udnævnt Professor. Ordstyreren giver Ordet og paaser, at Handlingen foregaar paa en værdig Maade; han kan paalægge en Opponent at høre op og i fornødent Fald afbryde Handlingen. Ordstyreren deltager ikke selv i Forhandlingen. Foruden de officielle Opponenten er de Medlemmer af Fakultetet, under hvis Fagomraade Afhandlingens Emne hører, og som ikke har lovligt Forfald, forpligtede til at overvære Forsvarshandlingen.
2. Som Opponenten ex auditorio har i Almindelighed kun akademiske Borgere samt polytekniske Kandidater Ret til at optræde. Dog kan Fakultetet ogsaa tillade andre, som fremsætter Ønske derom, at opponere. Opponenten ex auditorio maa melde sig hos Ordstyreren inden Begyndelsen af Handlingen; dog kan Ordstyreren ogsaa lade senere anmeldte Opponenten faa Ordet, men uden at betage dem, der tidligere har meldt sig, Forretten.
3. Der tilstaas i Almindelighed hver af de officielle Opponenten $1\frac{1}{2}$ Time og hver Opponent ex auditorio $\frac{3}{4}$ Time, derunder indbefattet den Tid, Doktoranden behøver til at give Svar; dog kan Ordstyreren, for saa vidt som Antallet af de anmeldte Opponenten tillader det, tilstaa en længere Tid. Handlingen maa ikke vare over 6 Timer.
4. Foranførte Bestemmelser skal indtil videre trykte medfølge enhver Disputats.

Dette bekendtgøres herved til Efterretning for alle Vedkommende.

Konsistorium, den 21. November 1927.

It is further demonstrated that blood sugar values above 0.200 % (up to 0.250 %) are fairly common in children under one year subsequent to ingestion of 2 gm. glucose per kg. (in 10 % solution) after a fasting period of 6—6½ hours.

With such a wide margin of physiological variations in infants, it is obvious that the course of the alimentary hyperglycæmia in infants has to be judged with a great deal of caution, before it is deemed to be pathological.

A survey of the findings in this group is given in Table 11.

Table 11.

*a. Uniform Glucose Tolerance Tests on 20 Infants (38 Tests).
(Age, 15 days to 1 year).*

	Average	Variations
Fasting values (46 exam.) ‰	0.080	0.067—0.101
Maximal values ‰	0.172	0.109—0.250
Rise of blood sugar ‰	0.091	0.023—0.165
Time of maximal value after glucose ingest. in min.	35	10—70
Duration of hyperglycæmia in min.	85	32—150

b. Individual Differences of Parallel Tests.

Differences in	Average	Variations
Fasting values ‰	0.010	0—0.022
Maximal values ‰	0.031	0.001—0.096
Rise of blood sugar ‰	0.031	0.002—0.105
Time of maximal value after glucose ingest. in min.	15	0—35
Duration of hyperglycæmia in min.	30	0—80

*c. Group III. Older Children.**(Age, 1—13 years).**Uniform Tolerance Tests.*

This group covers 22 children. As mentioned before, all these children were admitted for lesions which have presumably no influence upon the carbohydrate metabolism (their case-records are given in brief abstracts at the end of this section). The children were clinically well at the time the blood sugar examinations were made. No change was made in their diet during the examination period. In these tests the fasting period has been 14—15 hours. Two glucose tolerance tests (at an interval of 2—6 days) have been made in all the cases, excepting one (No. 11) where I did not have any opportunity to make more than one examination. The glucose was given in a dosage of 1.5 gram per kilogram of body weight (excepting No. 1, 5 and 7, who had 2 gm. per kg.), in the form of a 10 % solution. This dose was decided on as the middle between the standard dose for adults (1 gm. per kg.) and the dose employed for infants in this study (2 gm. per kg.). With the exception of a 1-year-old child, who had the glucose solution by way of stomach tube, the children drank the solution. None of them had any difficulty in taking the glucose solution, and they usually completed this act in 1—5 minutes.

In these examinations the average fasting value was 0.088 %, with variations from 0.068 to 0.099 %. The average difference between the fasting values in the same individual on two different days was 0.007 %. The greatest difference observed in the same child was 0.017 %, the smallest was 0.001 %.

The maximal values obtained were on an average 0.155 %, with variations from 0.122 to 0.201 %; and only in one instance did the value reach 0.201 %. In some instances the maximal value was reached as early as 5—25 minutes after the glucose ingestion, while in one instance it took 110 minu-

tes. The average time for the appearance of the maximal value was 36 minutes.

The duration of the hyperglycæmia was on an average 100 minutes. In one instance it lasted only 50 minutes. On the other hand, there were some instances where the fasting value was hardly reached at the end of the examination, $2\frac{1}{2}$ hours after the glucose ingestion (No. 12₁, Fig. 47; No. 19_{1,2}, Fig. 41; No. 21₁, Fig. 43; No. 22_{1,2}, Fig. 44).

The most frequent form of the hyperglycæmic curves is a rather abrupt rise to the maximal value within $\frac{1}{2}$ —1 hour, and then a fairly sudden fall with more or less pronounced after-rises, so that the primary hyperglycæmia is at an end in ca. 100 minutes (as found in both tests in No. 1 (Fig. 35), No. 13 (Fig. 38), No. 16 (Fig. 39), No. 20 (Fig. 42), No. 21 (Fig. 43)). In other instances, the abrupt rise is followed by a plateau — for about half an hour or more — and then a fall, usually without any after-rise. In No. 19 (Fig. 41) on both examinations, the blood sugar concentration is rising slowly for an hour before it reaches its maximum, respectively 0.148 and 0.147 %. In the first test there comes then a rather steep fall, with an after-rise, and again a fall to 0.114 %; in the next hour the blood sugar concentration varies between 0.110 and 0.120 %. In the second test there comes a gradual and slow fall after the maximum is reached; and here the last value is 0.119 %, which means that the hyperglycæmia is not at an end in either of these tests at the time the examination is discontinued. In No. 22 (Fig. 44) both tests show a gradual rise to the maximum, which is reached in 30—40 minutes, followed by a plateau of 30—40 minutes' duration, whereafter the fall is extremely slow, so that the fasting level is not reached in this case either when the examination is discontinued.

Hypoglycæmic values are seen in 4 tests (in No. 2, 6, 10, 12), varying between 0.023 and 0.032 % below the fasting value. No. 2 and 12 were sweating during the last half hour of the examination; when asked, both children complained of tiredness and hunger. In No. 2 the hypoglycæmic value is 0.062 % during the last 10 minutes of the examination period;

in No. 12 the blood sugar values are 0.056 and 0.043 %, likewise in the last 10 minutes of the period. No. 6 and No. 10 did not show any clinical signs of hypoglycæmia.

16 cases show a very marked similarity in the configuration of the curves from parallel tests, even though the maximal values are not the same (No. 1 (Fig. 35), 3, 5 (Fig. 36), 6, 7, 8 (Fig. 37), 9, 13 (Fig. 38), 15, 16 (Fig. 39), 17 (Fig. 40),

Blood sugar %

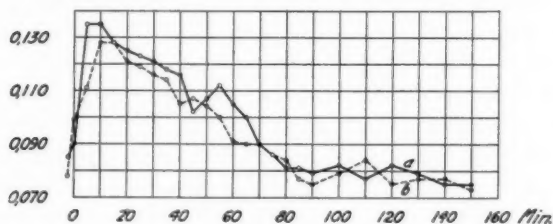


Fig. 35.

Group III. No. 1. Male, 13 mths. a, Jan. 6, 1930. 2 gm. glucose per kg.
b, » 9 » » » » » » »

Blood sugar %

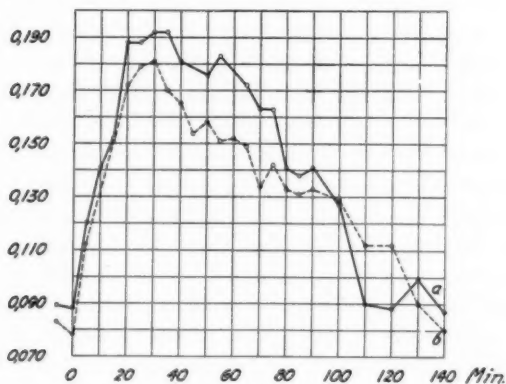


Fig. 36.

Group III. No. 5. Male, 3 y. 6 mths. a, Jan. 11, 1930. 2 gm. gluc. per kg.
b, » 16 » » » » » » »

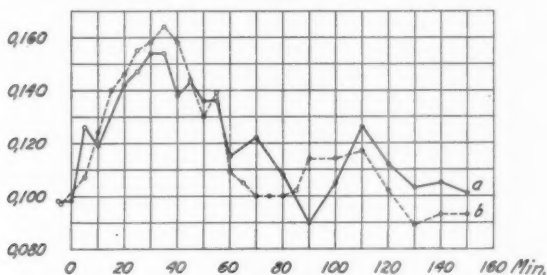
Blood sugar %

Fig. 37.

Group III.

No. 8. Female, 4 y. 4 mths. a, Sept. 26, 1930. 1.5 gm. gluc. per kg.

b, » 30 » » » » » » » »

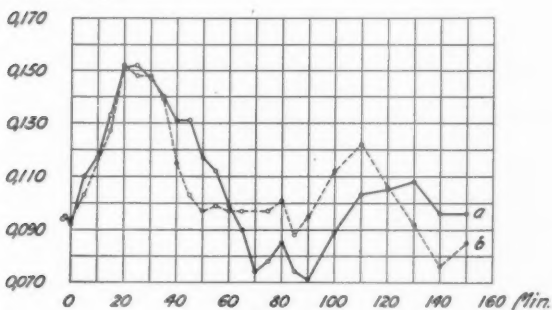
Blood sugar %

Fig. 38.

Group III.

No. 13. Female, 7 y. 2 mths. a, Nov. 13, 1930. 1.5 gm. gluc. per kg.

b, » 15 » » » » » » » »

18, 19 (Fig. 41), 20 (Fig. 42), 21 (Fig. 43), 22 (Fig. 44). The uniformity of the curves is particularly striking in No. 1 (Fig. 35), 21 (Fig. 43) and 22 (Fig. 44). 5 cases show a marked difference between the curves from parallel tests (No. 2, 4 (Fig. 45), 10 (Fig. 46), 12 (Fig. 47), 14 (Fig. 48). (Fig. 45—48 inclusive)), but No. 14 (Fig. 48) is the only case with any considerable difference between the maximal

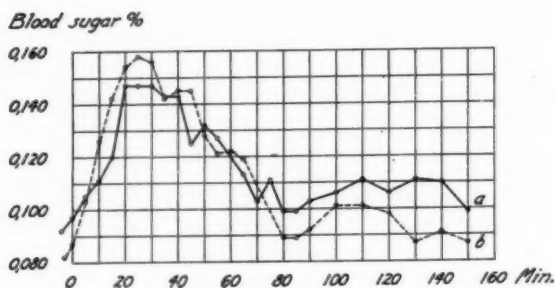


Fig. 39.

Group III. No. 16. Female, 8 y. 9 mths. a, Nov. 26, 1930.
Dose: 1.5 gm. gluc. per kg. b, » 29 »

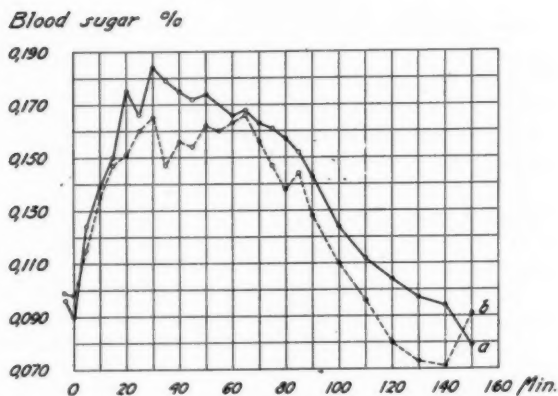


Fig. 40.

Group III. No. 17. Female, 9 y. 7 mths. a, Oct. 27, 1930.
Dose: 1.5 gm. gluc. per kg. b, » 30 »

values (0.034 %). In No. 4 both the curves are most irregular (Fig. 45).

The difference between the maximal values in the same individual is on an average 0.010 %, with variations from 0.000 to 0.034 %, whereas this difference in Group II (infants) was 0.031 %, with variations from 0.001 to 0.096 % and in

Blood sugar %

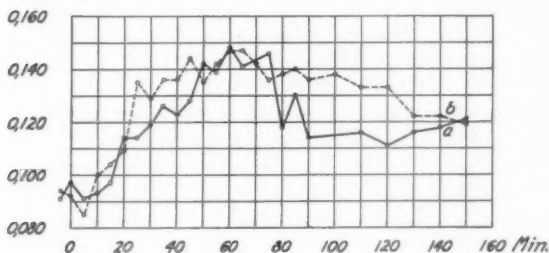


Fig. 41.

Group III. No. 19. Female, 12 y. 2 mths. a, Oct. 2, 1930.

Dose: 1.5 gm. gluc. per kg.

b, » 6 »

Blood sugar %

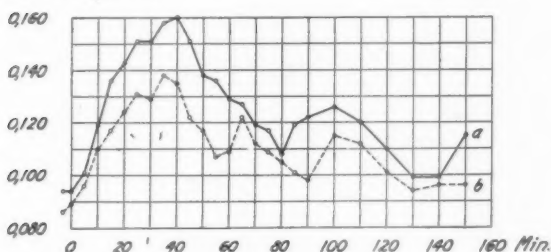


Fig. 42.

Group III. No. 20. Male, 12 y. 3 mths. a, Nov. 6, 1930.

Dose: 1.5 gm. gluc. per kg.

b, » 8 »

Group I (new-born) 0.031 %, with variations from 0.001 to 0.094 %.

As to the duration of the hyperglycæmia, the parallel tests show an average difference of only 14 minutes (in Group II it was 30 minutes), with 60 minutes as the greatest difference. In some of the cases there is no difference at all in the duration of the hyperglycæmia on the two tests.

From these findings it is evident that *even though parallel examinations after glucose ingestion in older children on different days do not show identical hyperglycæmic curves, their*

Blood sugar %

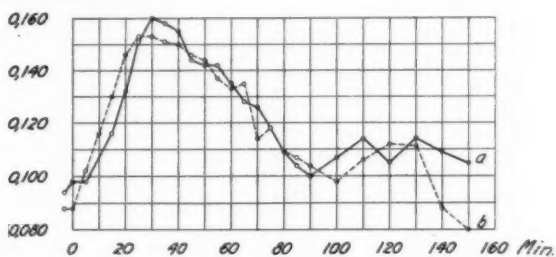


Fig. 43.

Group III. No. 21. Male, 13 y. 1 mth. a, Nov. 5, 1930
 Dose: 1.5 gm. gluc. per kg. b, » 7 »

Blood sugar %

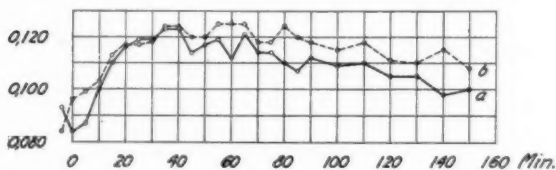


Fig. 44.

Group III. No. 22. Female, 13 y. 8 mths. a, Nov. 18, 1930.
 Dose: 1.5 gm. gluc. per kg. b, » 21 »

Blood sugar %

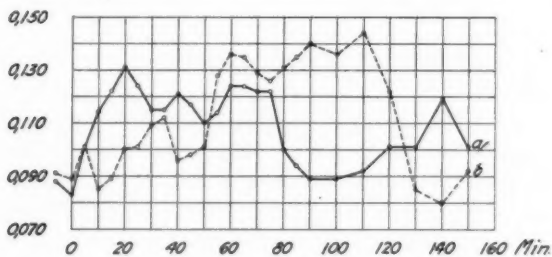


Fig. 45.

Group III. No. 4. Female, 2 y. 9 mths. a, Dec. 12, 1930.
 Dose: 1.5 gm. gluc. per kg. b, » 16 »

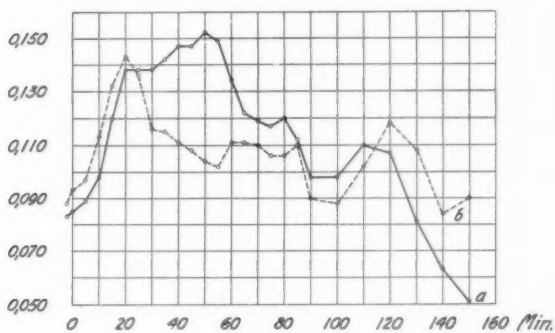
Blood sugar %

Fig. 46.

Group III. No. 10. Female, 5 y. 7 mths. a, Oct. 22, 1930.

Dose: 1.5 gm. gluc. per kg.

b, » 25 »

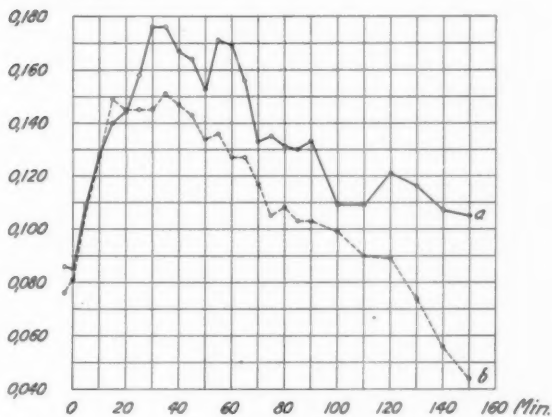
Blood sugar %

Fig. 47.

Group III. No. 12. Male, 6 y. 3 mths. a, Nov. 27, 1930.

Dose: 1.5 gm. gluc. per kg.

b, Dec. 1 »

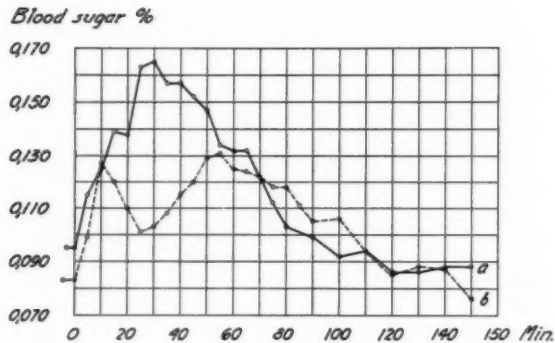


Fig. 48.

Group III. No. 14. Male, 7 y. 6 mths. a, Oct. 29, 1930.

Dose: 1.5 gm. gluc. per kg.

b, Nov. 1, 1930.

difference is still far less pronounced than that observed in infants (Groups I and II). Maximal values above 0.180 % are found only in 7 instances (No. 3₁₋₂, No. 5₁₋₂, Fig. 36; No. 17₁, Fig. 40; No. 18₁₋₂), and the highest maximal value is only 0.201 %, whereas values from 0.180 to 0.250 % are met with in half of the examinations in Group II. Putting everything together, these findings have established that in children from 1 to 13 years the alimentary hyperglycæmia after glucose ingestion takes about the same course as in adults. For in these children the average fasting value is 0.088 %, in variations from 0.068 to 0.099 %; and the average maximal value is 0.155 %, in variations from 0.122 to 0.201 %. As a rule the maximal value is reached in 30—60 minutes, and usually the hyperglycæmia is at end in less than 2 hours. Hypoglycæmic values occur now and then within the examination period — 2½ hours. After-rises are of frequent occurrence during the fall of the hyperglycæmic curve as well as after the fasting level has been reached.

Table 12 gives a survey of the findings in this group of children.

Table 12.

a. *Uniform Glucose Tolerance Tests on 22 Children (43 Tests).*
(Age from 13 months to 13 years and 8 months).

	Average	Variations
Fasting values %/.....	0.088	0.068—0.099
Maximal values %/.....	0.155	0.122—0.201
Rise of blood sugar %/.....	0.067	0.030—0.115
Time of maximal value after glucose ingest in min.....	36	5—110
Duration of hyperglycæmia in min.	100	50—>150

b. *Individual Differences of Parallel Tests.*

Differences in	Average	Variations
Fasting values %/.....	0.007	0.001—0.017
Maximal values %/.....	0.010	0—0.034
Rise of blood sugar %/.....	0.010	0—0.022
Time of maximal value after glucose ingest. in min.	13	0—90
Duration of hyperglycæmia in min.	14	0—60

Case-records of Group III.

No. 1. — Boy. Reg. No. 79/1930. Born, November 1, 1928.

1 $\frac{1}{4}$ year.

Adm. Jan. 3, 1930. Blood sugar exam., Jan. 6 and 9.

Disch. Febr. 14, 1930.

Clinical diagnosis: Anæmia. Oxyuriasis.

Hæmoglobin on admission: 65 %.

» Jan. 29 80 %.

Tp. normal. No symptoms of dyspepsia. Stools formed, perfectly normal.

Weight on adm. 8.300 kg.

» » disch. 8900 » + 600 gm.

No. 2. — Boy Reg. No. 618/1930. Born, June 11, 1928.

1½ year.

Adm. Nov. 27, 1930. Blood sugar exam., Dec. 13 and 17.

Disch. Dec. 21, 1930.

Clinical diagnosis: Angina tonsillaris. Bronchitis.

Tp. febrile during the first week after adm., then normal.

No symptoms of illness at the time of the blood sugar exam.

Appetite good. Bowels regular.

Weight on adm. 10.900 kg.

» » disch. 11.450 » + 550 gm.

No. 3. — Boy. Reg. No. 607/1930. Born, April 28, 1928.

1¾ year.

Adm. Nov. 20, 1930. Blood sugar exam., Dec. 11 and 15.

Disch. Dec. 17, 1930.

Clinical diagnosis: Tuberculosis latens. Colitis alimentaris.

Pirquet +. No abnormal X-ray findings. No elevation of temperature. On admission, the stools were somewhat mushy and stinking (Pt. adm. under the diagnosis: Dyspepsia chronica). After only a few days in hosp., the stools are normal and formed. Appetite good. After this, no symptoms of any illness whatever. Test meals show normal values.

Weight on adm. 15.500 kg.

» » disch. 16.550 » + 1.050 gm.

No. 4. — Girl. Reg. No. 620/1930. Born, March 1, 1928.

1⅔ year.

Adm. Dec. 8, 1930. Blood sugar exam., Dec. 12 and 16.

Disch. Dec. 23, 1930.

Clinical diagnosis: Vegetationes adenoid. Hypertrophia tonsillar.

Pt. has always been well, but lately she has been susceptible to

colds. On adm., the tonsils were markedly enlarged, and adenoids were found in the fauces. She was a little thin, with slight post-rachitic signs. Pirquet \div ; Mantoux \div . Appetite fairly good. Bowels regular. No rise of tp. On adm., the child weighed 11.900 kg., and during her stay in the hosp. her weight went up to 12.900 kg. After adenotomy and tonsillotomy (subsequent to the blood sugar exam.) her weight went down in 4 days to 12.150 kg.

Weight on adm.	11.900 kg.
» » disch.	12.150 » + 250 gm.

No. 5. — Boy. Reg. No. 31/1930. Born, July 22, 1926.

3¼ years.

Adm. Oct. 25, 1929. Blood sugar exam., Jan. 11, 16 and 20, 1930.

Disch. Jan. 21, 1930.

Clinical diagnosis: Tuberculosis gland. cervical.

On adm., the patient had a severe cold and was coughing a good deal. There was also some dyspnoea. Tp. was elevated the first days — around 39. On adm., the boy was pale, rather thin, showing slight post-rachitic signs. Bilateral swelling of the cervical glands — pea-sized. Pirquet \div ; Mantoux +. During the first 3 weeks the stools were sometimes rather slimy. Test meals showed normal conditions. No signs of any abnormality during the last 2 months in hosp.

Weight on adm.	13.350 kg.
» » disch.	14.500 »
	+ 1.150 »

No. 6. — Boy. Reg. No. 496/1930. Born, January 14, 1927.

3½ years.

Adm. Sept. 17, 1930. Blood sugar exam., Oct. 15 and 18.

Disch. Oct. 19, 1930.

Clinical diagnosis: Tuberculosis gland.

On adm., the boy was well nourished and looking healthy, showing but slight post-rachitic signs. Cervical and inguinal glands moderately enlarged. Pirquet +. No abnormal X-ray findings. The boy had a cold during his first week in hosp., when tp. was moderately elevated now and then. Appetite good. Bowels regular. No symptoms of any ailment at the time of the blood sugar exam.

Weight on adm.	14.400 kg.
» » disch.	15.150 »
	+ 750 gm.

No. 7. — Boy. Reg. No. 29/1930. Born, April 25, 1926.

3½ years.

Adm. Nov. 22, 1929. Blood sugar exam., Jan. 13 and 18, 1930.

Disch. Jan. 18, 1930.

Clinical diagnosis: Tuberculosis latens.

Complaints: Poor appetite; susceptibility to colds; fever now and then.

On adm.: Pale, rather thin and weak, with signs of previous rickets. Pirquet +. Hæmoglobin (on adm.) 81 %. X-ray exam. shows no abnormality. Test meals give normal values. Lack of appetite to begin with, later good appetite. Bowels regular throughout the stay in hosp. Tp.: at first, occasional subfebrile periods; no fever during the last 6 weeks, and no symptoms of any ailment in this period.

Weight on adm.	12.700 kg.
» » disch.	14.700 »
+	2.000 »

No. 8. — Girl. Reg. No. 459/1930. Born, May 27, 1926.

4¼ years

Adm. Aug. 26, 1930. Blood sugar exam., Sept. 26 and 30.

Disch. Oct. 3, 1930.

Clinical diagnosis: Tuberculosis hil. pulm.

Complaints: Tendency to fever and poor appetite.

On adm.: Well-developed, and well-nourished child. Pirquet +. X-ray exam.: Infiltration around the right hilus. Auscultation (repeated exam.): No abnormalities. Repeated exam. for tubercle bacilli ÷. Ewald test meal: Normal findings. Hæmoglobin 87 %. Tp. normal. Appetite good. Bowels regular. No symptoms of illness during her stay in hosp.

Weight on adm.	16.800 kg.
» » disch.	18.000 »
+	1.200 »

No. 9. — Girl Reg. No. 522/1930. Born, September 14, 1925.

5 years.

Adm. Oct. 11, 1930. Blood sugar exam., Oct. 21 and 24.

Disch. Oct. 31, 1930.

Clinical diagnosis: No abnormality.

Complaint: Poor appetite. She is an only child, much spoiled, who has been objecting to her meals for some time.

Physical exam.: No abnormality whatever.

She gives the impression of being rather nervous; otherwise, she is perfectly healthy. After a few days in the hosp., her appetite is very good. Bowels regular.

Weight on adm.	19.300 kg.
» » disch.	20.000 »
+	700 gm.

No. 10. — Girl. Reg. No. 523/1930. Born, March 6, 1925.

5½ years.

Adm. Oct. 15, 1930. Blood sugar exam., Oct. 22 and 25.

Disch. Nov. 2, 1930.

Clinical diagnosis: No abnormality.

The child is admitted for observation for tuberculosis. Before the adm. she had suffered from night-sweat, pains in the abdomen, alternating formed and loose stools, and subfebrile temperature.

Physical exam.: Well-developed and well-nourished child, with insignificant swelling of peripheral lymph glands. Pirquet÷; Mantoux ÷. No symptoms of any illness during her stay in hosp. Appetite good. Bowels regular.

Weight on adm.	20.000 kg.
» » disch.	22.000 »
+	2.000 »

No. 11. — Boy. Reg. No. 422/1928. Born, February 26, 1923.

5½ years.

Adm. September 24, 1928. Blood sugar exam., Oct. 18.

Disch. Oct. 21, 1928.

Clinical diagnosis: Tuberculosis latens.

Complaints: Periodic attacks of vomiting and diarrhoea; poor appetite.

Physical exam.: Thin but well-developed boy of healthy appearance. Abdomen normal. Pirquet +. A few days after adm. the patient is placed on full diet. Appetite good; stools perfectly normal.

Weight on adm.	16.200 kg.
» » disch.	18.600 »
+	2.400 »

No. 12. — Boy. Reg. No. 597/1930. Born, August 13, 1924.

6 years.

Adm. Oct. 30, 1930. Blood sugar exam., Nov. 27 and Dec. 1.

Disch. Dec. 18, 1930.

Clinical diagnosis: Adenitis colli. Tuberculosis latens.

Complaints: Tiredness and weakness.

On adm.: The child is rather thin, with swollen glands — size of hazelnuts — on both sides of the neck. Pirquet +.

X-ray exam.: No abnormality. Hæmoglobin 88 %. Ewald test meal: Normal findings. Tp. a little elevated the first week, normal the last 5 weeks. Pt. feeling perfectly well since the middle of November.

Weight on adm.	17.600 kg.
» » disch.	20.100 »
+	2.500 »

No. 13. — Girl. Reg. No. 573/1930. Born, August 30, 1923.

7 years.

Adm. Oct. 27, 1930. Blood sugar exam., Nov. 13 and 15.

Disch. Nov. 27, 1930.

Clinical diagnosis: No abnormality.

The patient was admitted for hysteria. At home she has frequent fits of rage, during which she was said to be quite unmanageable. The conditions in her home were unfortunate. In the hospital she made the impression of being perfectly normal mentally (excepting the first day) as well as physically (but she was rather thin). Her appetite was good; the bowels were regular.

Weight on adm.	17.100 kg.
» » disch.	20.000 »
+	2.900 «

No. 14. — Boy. Reg. No. 855/1930. Dep. D. Born, January 14, 1923.

7¾ years.

Adm. Oct. 21, 1929. Blood sugar exam., Oct. 29 and Nov. 1, 1930.

Disch. Nov. 2, 1930

Clinical diagnosis: Fractura cubiti sin. sequ. Contractura manus

In 1927, fracture of the left elbow. Subsequently paralysis of the radical nerve. Treatment for contracture of the fingers.

Otherwise perfectly normal.

Weight on exam. 22.200 kg.

No. 15. — Girl. Reg. No. 531/1930. Born, November 6, 1922.

8 years.

Adm. Sept. 30, 1930. Blood sugar exam., Oct. 14 and 17.

Disch. Nov. 7, 1930.

Clinical diagnosis: Obstipatio.

Complaint: Periodical tendency to constipation.

On adm. Large, well-developed and fairly well-nourished child of normal appearance. X-ray exam.: No abnormality.

Treatment with paraffin oil, by which the bowels became regular.

Weight on adm.	22.200 kg.
» » disch.	24.000 »
+	1.800 »

No. 16. — Girl. Reg. No. 595/1930. Born, February 15, 1922.

8½ years.

Adm. Nov. 7, 1930. Blood sugar exam., Nov. 26 and 29.

Disch. Dec. 10, 1930.

Clinical diagnosis: Bronchitis.

Past history: Frequent attacks of cold with coughing and rise of temperature. About one month before adm., severe coughing and loss of appetite. On adm.: Well-developed and fairly well-nourished child. Pronounced catarrhal symptoms.

Tp. elevated the first 6 days, then normal. Pirquet +.

X-ray exam.: No abnormality. Ewald test meal: Normal findings.

At the time of the blood sugar exam.: No signs of any ailment; appetite good; bowels regular.

Weight on adm.	22.000 kg.
» » disch.	25.800 »
+	3.800 »

No. 17. — Girl. Reg. No. 549/1930. Born, March 29, 1921.

9½ years.

Adm. Sept. 20, 1930. Blood sugar exam., Oct. 27 and 30.

Disch. Nov. 14, 1930.

Clinical diagnosis: Chorea minor.

Complaints: Early in 1930, the patient had a rather severe attack of chorea minor, for which she was admitted to this department, where she stayed 3 months. After this, she was well until 5 weeks before the admission, when she had a relapse.

On adm.: Small choreatic movements; otherwise no abnormality, especially no abnormality on auscultation of the heart.

The child was perfectly well 3—4 weeks before the blood sugar exam. Tp. normal throughout her stay in the hosp.

Weight on adm.	31.100 kg.
» » disch.	35.000 »
+	3.900 »

No. 18. — Boy. Reg. No. 421/1930. Born, August 2, 1920.

10 years.

Adm. July 22, 1930. Blood sugar exam., July 26 and Aug. 2.

Disch. Aug. 31, 1930.

Clinical diagnosis: Spina bifida occulta. Elongatio coli. Incontinentia alvi.

On adm. Looking healthy, but rather thin. X-ray exam.: Occult spina bifida.

To begin with, the boy had frequently involuntary bowel movement; this symptom disappeared on treatment with enema after every spontaneous evacuation. The mental habitus of the boy was normal. Neurologic exam. showed no abnormality.

Weight on adm.	22.100 kg.
» » disch.	24.400 »
+	2.300 »

No. 19. — Girl. Reg. No. 464/1930. Born, July 21, 1918.

12 years.

Adm. Sept. 13, 1930. Blood sugar exam., Oct. 2 and 6.

Disch. Oct. 6, 1930.

Clinical diagnosis: Dyspepsia. Tuberculosis gland.

Complaints: Frequent attacks of diarrhoea; now and then; vomiting; poor appetite; loss of weight.

Physical exam.: Well-developed, but rather thin; moderate swelling of the cervical lymph glands (pea-size); otherwise no abnormality.

To begin with, the stools were sometimes formed, sometimes thin. The appetite was good. There was no nausea or vomiting, no pains and no intumescence of the abdomen. The stools became normal as early as 6 days after the adm., and remained so throughout. The girl

appeared to be perfectly well and normal the last 3 weeks of her stay in the hosp. She was on full diet.

Weight on adm.	28.700 kg.
» » disch.	29.600 »
+	900 gr.

No. 20. — Boy. Reg. No. 535/1930. Born, August 2, 1918.

12 years.

Adm. Oct. 28, 1930. Blood sugar exam., Nov. 6 and 8.

Disch. Nov. 9, 1930.

Clinical diagnosis: Albuminuria orthostatica.

Complaints: Frequent spells of tiredness and headache, now and then with subfebrile temperature. The family physician had demonstrated albumin in the morning urine.

On adm. Delicate appearance; marked lordosis and scapulæ alatae. Pirquet ÷. Hæmoglobin 82 %.

Urine: Morning portion, ÷ Alb.; after the patient had been up some hours, + Alb. Microsp. exam. shows no abnormality.

Weight on adm.	33.200 kg.
» » disch.	34.000 »
+	800 gm.

No. 21. — Boy. — Reg. No. 871/1930. Dep. D. Born, September 28, 1917.

13 years.

Adm. Sept. 13, 1930. Blood sugar exam., Nov. 5 and 7.

Disch. Nov. 8, 1930.

Clinical diagnosis: Fractura cruris sin.

Present illness: Fracture of the left leg on the day of adm.

Oct. 25. Firmness at the site of the fracture. No complication whatever (Sept. 14. Urine: ÷ sugar).

Apart from the fracture, the boy has been perfectly well through out his stay in the hosp.

Weight on exam.	32.100 kg.
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No. 22. — Girl. Reg. No. 575/1930. Born, March 28, 1917.

13½ years.

Adm. Nov. 12, 1930. Blood sugar exam. Nov. 18 and 21.

Disch. Nov. 28, 1930.

Clinical diagnosis: Obstipatio.

Complaint: For several years, frequent spells of constipation.

On adm.: Large, well-developed child, with beginning signs of puberty. No abnormality. Hæmoglobin 86 %. Pirquet ÷.

Ewald test meal: Normal findings. Bowel movement regular after paraffin oil.

Weight on adm.	42.800 kg.
» » disch.	42.150 »
÷	650 gm.

d. COMPARATIVE EXAMINATIONS AFTER DIFFERENT DOSES OF GLUCOSE.

Previous Investigations.

Mention has been made previously of the acceleration phenomenon described by K. M. Hansen⁴⁵, which designates the fact that the blood sugar concentration rises only to a certain limit even after very large doses of glucose. At this upper limit of the blood sugar concentration the elimination of the sugar from the blood stream is »accelerated«, so that the blood sugar concentration is not increased further. In adults, K. M. Hansen finds this limit to fall at ca. 0.180 %, even after doses as large as 400 grams of glucose.

Herlitz⁵⁰ has made some examinations of this point on children. To 14 normal infants he gave 4—7 gm. glucose (in 100 cc. water) per kilogram of body weight; and in three of these cases he found the maximal blood sugar value to be 0.207, 0.221 and 0.242 % (after ingestion of 5, 6 and 5 gm. glucose per kg.). The lowest maximal value in this series was 0.135 % after 6 gm. glucose per kg. The average maximal value was 0.183 %, whereas 21 children, who had 1.3 gm.

glucose per kg., showed an average maximal value of 0.123 %, with variations from 0.110 to 0.162 %. (From the tables of Herlitz it looks as if the two series of examinations are not carried out on the same children). So in the majority of his cases, Herlitz found the maximal blood sugar values considerably higher after the large doses of glucose than after the smaller doses. Yet he concludes (cf. p. 30) that ingestion of large doses of glucose in normal infants gives, as a rule, hyperglycæmic conditions comparable to the findings in adults under analogous conditions. In this conclusion, however, he leaves out the three instances of particularly high blood sugar concentration as being deviations from the rule.

Mertz & Rominger⁸⁰ (cf. p. 29) may also be quoted in this connection. They examined the blood sugar in 17 children, whom they gave 30—50 gm. glucose regardless of their weight, making the doses as variable as 3—15 gm. per kg. The maximal values obtained in this way were generally less than 0.200 %. Yet in 3 cases the maximal value was 0.208, 0.295 and 0.261 %; in the last two of these cases, the dose was respectively 9 and 14 gm. per kg.

Own Investigations.

In 6 children I have examined the blood sugar concentration after varying doses of glucose, each child being submitted to two or several examinations. 5 of the children were less than 1 year, one was 3½ years. The maximal values obtained in these tests are given in Table 13, p. 88. Only in 2 cases does the dose exceed 2 grams; for the rest it is 1 or 2 gm. per kg.

It will be noticed that in one case (b. No. 1, Fig. 49) the values are about alike after 1 and 2 grams of glucose, whereas the blood sugar concentration rises considerably higher after 6 gm. In the remaining 4 cases examined with 1 and 2 gm. glucose, the blood sugar rise is considerably higher after 2 gm. than after 1 gm. (Fig. 50). In one case (b. No. 13, Fig. 51), a child of 5 months, 2 tests with 2 gm. glucose per kg. gave a maximal value of 0.249 and 0.153 % respectively. Tests with

Table 13.
Maximal Blood Sugar Values after Different Doses of Glucose.
(For dates of examination and other details, see the respective protocols).

Age	Case No.	Dose of glucose per kilogram of body weight				
		1 gm.	2 gm.	4 gm.	6 gm.	10 gm.
2—5 weeks.....	No. 1 (Group II)	0.133	0.110			
		0.118	0.138		0.165	
1 ³ / ₄ —2 months	No. 1 (Protocols Gluc. — Sac.)	0.151	0.208			
5—6 months	No. 13 (Group II)		0.249	0.215	0.250	0.225
			0.153			
6 ¹ / ₂ —9 months	No. 5 (Protocols Gluc. — Sac.)	0.110	0.189			
9 months	No. 16 (Group II)	0.124	0.173			
		0.142	0.184			
3 ¹ / ₂ years	No. 5 (Group III)	0.155	0.192			
			0.181			

4, 6 and 10 gm. glucose — on the same child — gave maximal values of 0.215, 0.250 and 0.225 % respectively. This shows that the maximal blood sugar value after all the 4 different doses may vary within the same limits.

As to the duration of the hyperglycaemia, with 1 gram of glucose it was 60—110 minutes, after 2 grams it was 60—130 min. After 4 and 6 grams of glucose the hyperglycaemia lasted 80—100 min., and after 10 grams (one test) only 60 min. So the durations of the hyperglycaemias after the different doses of glucose are also falling within the same limits.

If these few tests allow of any conclusion whatever, it will be this, that *the acceleration phenomenon does also appear in children, but probably at somewhat higher blood sugar values*

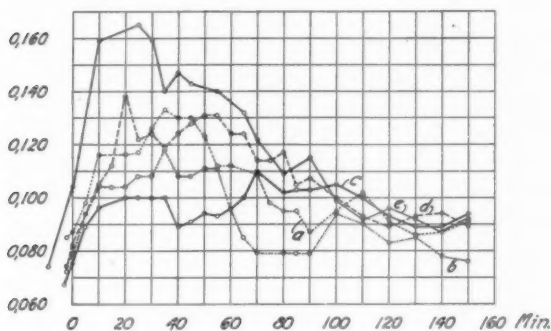
Blood sugar %

Fig. 49.

b. No. 1. Female, 26 days — a, July 12, 1929. 1 gm. gluc. per kg.
 (Group II) 30 » — b, » 16, » 1. » » » »
 15 » — c, » 1, » 2 » » » »
 20 » — d, » 6, » 2 » » » »
 33 » — e, » 19, » 6 » » » »

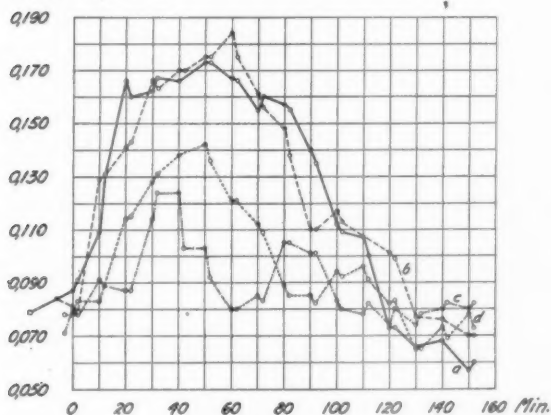
Blood sugar %

Fig. 50.

b. No. 16. Male, 9 months. a, Nov. 9, 1928. 2 gm. gluc. per kg.
 (Group II) b, » 12, » 2 » » » »
 c, » 19, » 1 » » » »
 d, » 23, » 1 » » » »

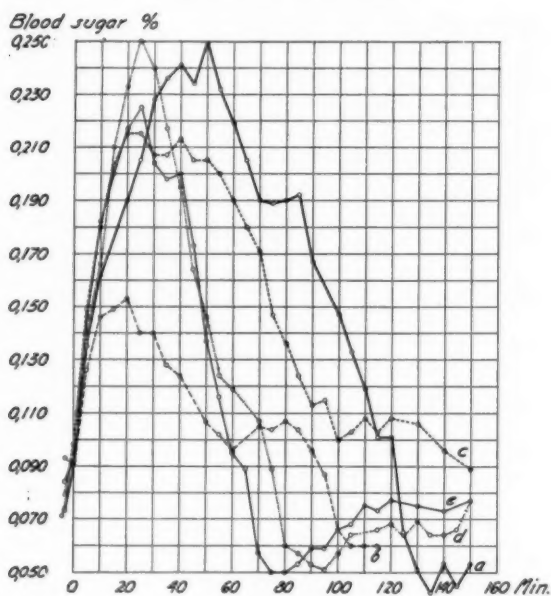


Fig. 51.

b. No. 13. Male, 5—6 months.	a, April 30, 1929.	2 gm. gluc. per kg.
(Group II)	b, May 4, »	2 » » » » »
	c, » 10, »	4 » » » » »
	d, » 14, »	6 » » » » »
	e, » 23, »	10 » » » » »

— above 0.200 % — than in adults. This, I think, is also suggested in the findings of Herlitz⁵⁰; and the results of Mertz & Rominger⁵⁰ may be interpreted along the same lines.

e. COMPARATIVE EXAMINATIONS AFTER INGESTION OF GLUCOSE AND SACCHAROSE.

Previous Investigations.

Several studies have been reported on the rise of the blood sugar concentration in children after ingestion of sugars other than glucose. Here, however, mention will be made only of

investigations dealing with the blood sugar after saccharose ingestion.

Frank & Mehlhorn³¹ (1920) gave a dose as large as 8 grams of saccharose per kilogram of body weight in 200 cc. of tea (blood-taking every 30 minutes, Bang's micromethod for sugar determination). Under these conditions they found a rise of the blood sugar concentration up to 0.200 % within 30—60 minutes; and the duration of the hyperglycæmia was 6 hours. Flood²⁹ (1924) has examined the blood sugar in children under 14 days after ingestion of various sugars, including glucose and saccharose. But, this author uses venous blood for his sugar determinations, and he makes only 2—3 determinations in a couple of hours. Moreover, he has not employed the same children in testing the effects of the different sugars. So his findings do not allow of any conclusions.

Styrikowitsch¹¹⁴ (Hagedorn-Jensen's method, and blood-taking every 15 min. for 2½ hours) has examined the blood sugar in 12 new-born (3—4 days old) after ingestion of 2 grams of »beet-sugar« — presumably saccharose — per kilogram of body weight (in 10 % watery solution). The maximal value was reached, on an average, in 58 minutes, and the rise did not amount to more than 59 % of the fasting value. In several instances the blood sugar curve stayed at the level of the maximum through the rest of the examination period, but in general the hyperglycæmia was at an end in about 100 minutes. Styrikowitsch has thus found a slow rise of the blood sugar concentration and a low maximal value, besides in several instances a protracted duration of the hyperglycæmia (cf. my findings after glucose ingestion in Group I, p. 45).

Greenwald & Pennel³⁷ (1930) (Folin's micromethod) studied the blood sugar in 60 children, aged 2—10 days, after ingestion of glucose, lactose, saccharose, and dextromaltose — the dose being 2 grams per kilogram of body weight, in a 20 % watery solution. These authors made 15 tests with each sugar, but they too gave the various sugars to different children; and furthermore the blood samples were

taken only every 30 minutes for 2 hours, so their findings are to be accepted with reservation. They conclude that the best absorption (by this they mean the greatest rise of the blood sugar concentration) takes place after ingestion of glucose, then after saccharose, lactose, and dextromaltose. Their curves show that glucose gives the highest blood sugar rise — on an average, 0.115 % in 1 hour — while saccharose gives a rise of 0.114 %, lactose 0.112 %, and dextromaltose 0.102 %.

Own Investigations.

On 6 children, aged 1—8 months, tolerance tests are made at intervals of 2—19 days, with 2 gm. glucose and with 2 gm. saccharose per kg. of body weight, in 10 % watery solution. In one case (No. 1, Fig. 52) there was no essential difference between the maximal values obtained with glucose and with saccharose (glucose 0.007 % above saccharose), and in confi-

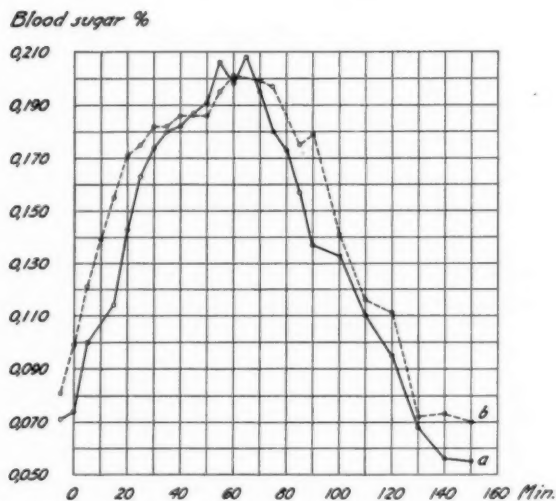


Fig. 52.

No. 1. Male, 2 months, a, May 19, 1928. 2 gm. gluc. per. kg.
b, » 21, » 2 » sacch. » »

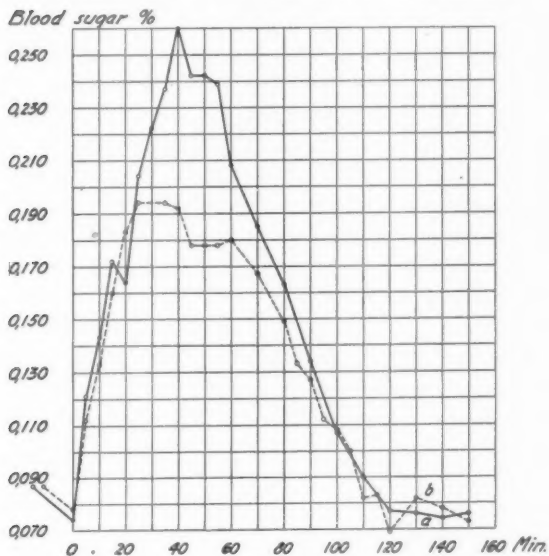


Fig. 53.

No. 3. Male, 2 months. a, May 5, 1928. 2 gm. gluc. per kg.
b, » 12, » 2 » sacch. » »

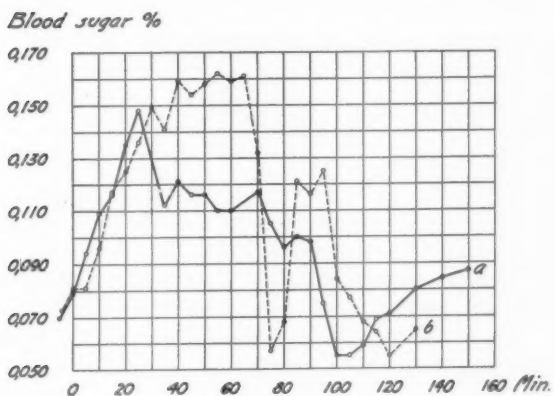


Fig. 54.

No. 4. Male, 6 months. a, May 18, 1928. 2 gm. gluc. per kg.
b, June 6, » 2 » sacch. » »

guration the two blood sugar curves were also very much alike. In 4 cases the blood sugar rise was greater after glucose ingestion than after saccharose, the respective differences being 0.015, 0.047, 0.051 and 0.066 (Fig. 53); in one case (Fig. 54) the blood sugar rise was greater after saccharose (0.024 %). The highest maximal value after glucose ingestion was 0.260 %; after saccharose ingestion it was 0.201 %. There was no essential difference in the configuration of the blood sugar curves nor in the time for the appearance of the maximal values, which took place as a rule in $\frac{1}{2}$ —1 hour.

From these — few — tests it appears as if *the hyperglycæmia is generally somewhat greater after glucose ingestion than after saccharose. This is no established rule, however, as the reverse as well as practically identical maximal values are found too.*

Table 14.
Parallel Tolerance Tests with Glucose and with Saccharose.
(6 children, aged 1—8 months, 12 tests with 2 gm. per kg.).

	Average ‰	Variations ‰
Fasting values (14 determin.)	0.080	0.062—0.089
Difference of fasting values in the same individual	0.009	0—0.023
Maximal values — glucose	0.191	0.146—0.260
Maximal values — saccharose	0.163	0.131—0.201
Rise of blood sugar — glucose	0.113	0.070—0.173
Rise of blood sugar — saccharose	0.082	0.042—0.107
	Glucose	Saccharose
Time of maximal value (min.)	10— 65	10— 60
Duration of Hyperglycæmia (min.)	90—120	60—130

III. BLOOD SUGAR IN SICK CHILDREN.

In the following I shall report some examinations on the blood sugar regulation in various diseases.

My attention has been drawn in particular to the question of the blood sugar regulation in patients with coeliac disease.

I was rather late in taking up a study on the behaviour of the blood sugar in myxoedema patients before and after treatment with thyroidin, so I have as yet but a few examinations to report on this question. I trust, however, that I shall be able in a subsequent paper to return to this interesting subject. Finally, the blood sugar regulation has been examined in rickets, tetany and infantile eczema (exudative diathesis, Besnier's prurigo) to check up the views and findings put forth by other investigators. In the examination of these patients, my technique has been essentially the same as that employed in the examination on normal children. Whenever the technique has been modified, this is stated in each case.

I have not made any study into the blood sugar regulation in diabetic children, as I have considered such investigations falling outside the scope of this paper. The same applies to studies on the blood sugar regulation in febrile conditions.

1. COELIAC DISEASE.

*A. Clinical Aspects.**Previous Authors.*

The disease was first described by Gee³⁵ under the name »coeliac affection«. Later it was described in detail by Herter⁵¹ who named it »Infantilismus intestinalis«, and by Heubner,⁵² who discussed it under the title »Schwere Verdauungsinsufficiens beim Kinde jenseits des Säuglingsalters«. Subsequently this lesion has been the subject of numerous clinical papers, amongst others, by Bauer,⁴ Bloch,^{9,10} Freise & Jahr,³² Fröhlich,³³ Kundratitz,⁶⁵ Lehdorff & Mautner,⁶⁹ Lichtenstein,⁷⁰ Miller,⁸² Pipping,⁹⁴ Sauer,¹⁰⁰ Schick & Wagner,¹⁰¹ Schütz,¹⁰³ Stolte,¹¹² and Taylor¹¹⁶.

The *clinical features* of the lesion are now established fairly well. As a rule, the disease makes its appearance after the first year of life, and it is never observed in unweaned breast-babies. Often the first symptoms of the lesion are preceded by some severe infection — for instance, whooping-cough, influenza, or acute gastro-enteritis. In other cases, the disease comes on insiduously, without sign of any other lesion in the past. The child begins to look sickly, lose its appetite and fall off in weight; at the same time, the bowels become irregular, and there are periods with thin foamy stools alternating with periods of constipation. When the disease is fully developed, its cardinal symptom is voluminous, spongy, foamy and stinking, greyish-white stools containing large amounts of fat. The child is stunted in its growth and emaciated, with poor and flaccid muscles, in particular flattened buttocks (a symptom that has been emphasized especially by Miller⁸³); besides, the turgor of the skin is markedly impaired. Often the weight of the patient is subject to wide variations from hydrolability; and there is frequently a tendency to oedema which is neither of cardiac nature nor of renal origin, but rather in kind with hunger oedema. Further, there is often a tendency to extravasation of the blood. Tetany, more or less latent, is present in a great majority of the cases. Often these

patients show changes in the bones — particularly halisteresis, or changes resembling rickets — as pointed out by Parson^{9a}. Bloch¹⁰ emphasizes the resemblance to those forms of rickets that are characterized by hypocalcæmia and osteoporosis while the cartilage proliferation is only slight. He thinks that the rickets of these patients as well as the accompanying tetany are due to defective absorption of calcium compounds from the intestinal canal.

Mentally, these children are not lagging, as a rule, but they are frequently irritable and fitful. It is sometimes claimed that these children are neuropathic; but their nervousness may just as well be interpreted as secondary results of the coeliac disease and its complications, especially tetany.

Some authors state that coeliac disease is met with most frequently among the children of the well-to-do. This assertion has been contested with the argument, that this distinction is only apparent because children living under less favorable conditions are more apt to die before the disease is fully developed.

The prognosis is doubtful. The course of the lesion is extremely chronic, sometimes going on for a number of years, but as a rule the patients die in adolescence from progressive cachexia or intercurrent disease, to which they are particularly susceptible, their resistance being greatly lowered from their protracted illness. In case of recovery, as emphasized by Bloch,¹⁰ one will sometimes wonder whether there might not have been a mistake of diagnosis — that is, whether it might not have been a case of chronic colitis, as the differential diagnosis between this and coeliac disease may be very difficult. Apart from this, the differential diagnosis involves in particular the ruling-out of abdominal tuberculosis and pancreaticogenous fatty diarrhoea.

As to the *etiology* of coeliac disease, the views of various investigators are widely divergent. Herter⁵¹ thought that the lesion is due to a chronic inflammation of the gut produced by an intestinal flora, resembling the bacterial flora in normal infants but different from the intestinal flora in older children.

Other authors — Heubner⁵² et al. — have had similar bacterial findings, but they have not attributed any etiological significance to these findings. Brown, Courtney, Davis & Mac Lachlan¹³ have isolated a spore-forming bacillus from the faeces in some cases; when cultivated in milk and fed to rats, these bacilli were said to cause a cessation of the growth in these rats. Fröhlich³³ and a few others have attached particular importance to the fact that scorbutic symptoms are frequent in these patients, and they have therefore interpreted the lesion as being an avitaminosis. Bloch^{9,10} points out that in its beginning the lesion does not show any points of resemblance to any of the established forms of avitaminosis; and he looks upon the subsequent signs of avitaminosis as secondary concurrent phenomena. Miller⁸² holds that the lesion is connected with a disturbance of the function of the bile salts in the process of digestion. On the other hand, he finds no deficiency of bile pigment, the light colour of the faeces notwithstanding, the presence of bile pigment being merely concealed by the large amounts of fats.

Several authors agree in interpreting the lesion as a constitutional weakness, involving the organism as a whole and especially the digestive tract, and manifesting itself when the functional capacity of the organism is strained by an infection or by the added demands implied in artificial feeding instead of mother's milk (Freise & Jahr³², Heubner⁵², Fanconi²⁷, Pipping⁹⁴).

Particular stress has often been laid upon the fact that the respective child has a family history of neuropathic conditions, and that it shows itself some nervous symptoms. Thus, Fanconi²⁷ is inclined to regard the lesion as contingent upon a »vegetative neurosis, a vagotonia«, as a feature of a general constitutional weakness of the nervous system.

The clinical picture of the patients may be suggestive of endocrine disturbances. This seems indicated by the marked retardation of the growth, by the frequency of abnormal pigmentation and abnormal hairiness and by the sometimes remarkably low blood pressure (cf. case-records No. 1

and 2). There is, for one thing, some resemblance to Addison's disease — as has also been pointed out by Mac Lean & Sullivan ⁷⁶. A low alimentary blood sugar curve has been described as occurring, though not regularly, in Addison's disease, and, as will be pointed out later on, this is a feature common to Addison's disease and coeliac disease. There is further a great deal of resemblance between coeliac disease and sprue (in which the etiology is obscure, too). Common to these two lesions are the peculiar character of the stools, the frequency of spasmophilia and the marked debilitation of the muscles. Thaysen ¹²⁰ who has made a very thorough study of sprue — especially the non-tropical sprue — is of opinion that this lesion, too, may involve some endocrine disturbances.

Autopsy has not revealed anything essential to clear up the etiology of coeliac disease. The various cases have shown very different changes in the organs that are largely to be explained as secondary phenomena resulting from the gradually developing cachexia. Clarke & Hadfield ¹⁹ have found marked atrophy of the pancreas with fatty infiltration, showing only a scanty amount of secreting tissue but with a relatively large number of Langerhans islands. Similar findings have been reported by Gross ⁴¹. Burghard ¹⁸ finds cystic degeneration of the pancreas. Kundratitz ⁶⁵ finds marked fatty infiltration of the liver and, to a less degree, the other endocrine glands. Pipping ⁹⁴ finds fatty infiltration of the liver; Schick & Wagner ¹⁰¹ report a marked atrophy of nearly all the endocrine glands.

Bloch ⁰ has examined two cases in which post-mortem changes were prevented by injection of 10 per cent formalin solution into the stomach and the abdominal cavity shortly after death. The examination showed none of the changes mentioned above, but a subacute inflammation of the stomach and intestines. The secretory cells in the mucous membrane of the stomach contained only a few granules. The wall of the colon was studded with large goblet cells. The parathyroids showed no abnormality (there had been tetany in one of these cases); nor were any changes made out in the other endocrine glands.

Examination of the *metabolism* in coeliac disease has not given uniform or conclusive results concerning the etiology of the lesion. Fanconi ²⁷ has made a comprehensive study of this question, with a view to several branches of the metabolism. In severe cases of coeliac disease he finds some very marked changes in the mineral contents of the blood, especially a decrease of calcium and phosphorus; he also finds a decrease of the serum albumin. He lays particular stress upon the hydro-lability of these children; and he states that the alimentary lipæmia is retarded in its appearance and lower than normal. Fanconi ²⁶ has also made some blood sugar examinations in these cases, but he does not report the technique employed, the fasting period preceding the glucose ingestion or the glucose dosage in proportion to the weight of the children. He mentions an increase and protraction of the blood sugar curve which he attributes to a decrease of absorption power. It appears as if he has taken but one or two blood samples in each examination, so his findings do not allow of any conclusions. In contrast with this author, Moncrieff & Payne ⁸⁵ find an increase of the alimentary lipæmia, and from this they think it warrantable to conclude that the great fat content of the fæces is not due to a deficiency in the absorption of the fats of the food but to an elimination of fat from the blood. Also on a low fat diet do they still find a rather plentiful elimination of fat. Similar findings are reported by Miller ⁸².

In cases where the lesion has been accompanied by tetany, Bloch ¹⁰ has found a decrease in the serum calcium.

In most of the cases, gastric test meals show normal acid values; now and then there is achylia or hypochylia. The duodenal juice shows a normal content of enzymes. No definite abnormality has been demonstrated in the composition of the bile. In functional liver tests with galactose, Taylor ¹¹⁶ has found but normal conditions.

Schütz ¹⁰³ has found connective tissue strands in the stools after the Schmidt meal, and he takes this to signify a disturbance of the gastric digestion.

An increase of the intestinal putrefaction has been found

in many cases — first by Herter⁵¹ who demonstrated the presence of absorbed products of intestinal putrefaction in the urine.

All authors have reported an abnormally large output of fats in the faeces, in which the dry substance may consist of 50—60 per cent of fat. Schick & Wagner¹⁰¹ state that the greater part of the fat is split into fatty acids and soaps, but often the soaps make only 5—10 per cent of the total amount of fats. Still, even with a relatively small percentage of saponified fat, the absolute amount of calcium soaps is quite large on account of the excessive total amount of fats, a point that is also emphasized by Schick & Wagner. Harrison & Sheldon⁴⁷ have made a very large number of faeces analyses in cases of coeliac disease, and they state that the percentage of total fat in the faeces is exceedingly high; often they too find the total fat content as high as 50—60 per cent, whereas the proportion between split and unsplit fat is normal. They emphasize that differential analysis of the fat fractions in faeces, therefore, cannot give results pathognomonic of coeliac disease, and that the absolute amount of fat is the criterion in the differential diagnosis. For, if the total fat content of the faeces in a non-treated case falls within the normal limits, it is unlikely that the case is one of coeliac disease.

For comparison the normal values shall be referred to. Schick & Wagner¹⁰¹ state that the normal fat content of faeces amounts to 10—25 %, and that 20—25 % of the total fat is neutral fat while the rest is about equally divided in free fatty acids and soaps. Harrison & Sheldon⁴⁷ quote from Holt, Courtney & Fales that in children from 1 to 7 years, on ordinary mixed diet, the total fat content of the faeces averages ca. 19 %, and that ca. 27 % of this is unsplit neutral fat. In infants, the fat content of the faeces is somewhat greater, 30—35 %, in breast-babies as well as bottle-babies. Harrison & Sheldon hold that the greater significance should be attached to the proportion between split and unsplit fat (the term »split fat« implying both free fatty acids and soaps), whereas, they think, the proportion between free fatty acids and saponified

fatty acids is subject to great variations in normal individuals too. They emphasize that the proportion between split and unsplit fat is an indication of the efficiency of the fat digestion while the total fat content gives a measure of the fat absorption.

As to the treatment, Gee³⁵ already points out that cow's milk is directly injurious to these patients. All subsequent authors have subscribed to this finding. On the other hand, several authors — Heubner⁵², Lichtenstein⁷⁰, et al. — have found that woman's milk agrees very well with these patients, so it has been given even to big children. Bloch⁹, however, has not found any favorable results from woman's milk.

Now it is generally agreed that the diet of such children should be abundant in vitamins, poor in fat and rich in protein, and that ripe bananas form a very suitable food for these patients. As to the carbohydrates of the diet, opinions differ. In this department we have profitably used a diet advocated by Kerley⁶². The chief constituent of this diet is a barley gruel containing ca. 8 % casein, 8 % starch and 8 % cane-sugar. In addition to this, the patient gets crackers, toast, plenty of fruit, especially bananas, purees of vegetables, and, later, minced meat, and a little butter.

Own cases.

5 children with coeliac disease, whom I have had an opportunity to examine, all showed a very typical and marked degree of the lesion. In all five children the abdomen was large and distended, forming a striking contrast to the thin extremities with their flaccid muscles (Fig. 55). The stools were voluminous, fatty, spongy and stinking. All the patients were stunted in growth (but hardly in mental development, though the illness had naturally produced some irritability). In all of them the disease ran an afebrile course, the only, slight, rise of temperature observed a couple of times being associated with colds. All the patients were showing signs of

present or previous rickets, and all had caries of the teeth. As a rule, they showed a slight degree of simple anæmia, but



Fig. 55.

Coeliac disease. Case No. 1.

Distended abdomen, flabby muscles.

no blood changes resembling pernicious anæmia; and there was no glossitis — a condition often observed in sprue. In none of these cases did the urine show any abnormalities.

In three of these children (No. 3, 4 and 5) the parents thought that the onset of the lesion might be connected more

or less with an infectious disease; in the case of No. 3 this was whooping cough, in No. 4 and 5 it was influenza. No. 1 gave a



Fig. 56.

Coeliac disease. Case No. 1.
Flattened and wrinkled buttocks.

history of severe bronchitis a couple of years before the first symptoms of the lesion were noticed. No. 2 showed a positive tuberculin reaction.

I may here point out a couple of symptoms observed in some of these patients. No. 1 and 3 showed peculiar pigmen-

tions of a brownish-grey dirty colour, resembling the pigmentation in Addison's disease. These pigmentations were most pronounced on the parts exposed to the light — face and hands — and they were also present on the back, breast and abdomen and in the axillæ. But no pigmentation was observed on the mucous membrane of the cheeks. Conspicuous lanugo was present in No. 1, 2 and 4; in No. 1 the hairiness of the lip was so pronounced as to remind of a little moustache. This symptom has not been mentioned by any other author, as far as I know.

No. 1, 3 and 5 showed distinct symptoms of tetany; and in No. 2 and 5 there were signs of avitaminosis (scurvy, conjunctival xerosis). The symptom emphasized by Miller⁸³ — peculiar flattened and wrinkled buttocks — was present in No. 1, 2 and 3 (Fig. 56).

The results of the fæces analysis in 4 of the cases are given in Table 15 p. 106. This analysis covers samples of fæces collected during a period of 3 days while the patients have been on a controlled diet. The fæces from this period were marked by means of carmine tablets.*)

From these analyses it is evident, then, that even when placed on a fat-free diet, the patients evacuate rather considerable amounts of fat (12.95—31.20 %), a fact that is also emphasized by previous authors (Miller⁸² et al.).

When fats were supplied, more than half of the dry substance of the fæces, as a rule, consisted of fats — whereas in normal individuals the fat content of the fæces on this diet is 20—25 % of the dry substance. Usually this fæcal fat was split in normal proportion, only $\frac{1}{3}$ or less being present as neutral fat. Still, in a couple of cases, the fat consisted in almost equal parts of neutral fat and split fat. The proportion between free fatty acids and soaps was, on an average, so that the free fatty acids made a considerably larger portion than the soaps; but, on the whole, this proportion was subject to

*) These analyses have been made by Struer's Laboratory.

Table 15.
Fæces Analysis in Coeliac Disease.)*

(In each case the analysis is made on the total fæces collected in a period of 3 days, in which the given diets were kept).**)

No. 1.

	Fat-free diet.	Fat-free diet. + 100 gm. butter on 1' day 60 gm. butter 2' and 3' day	Fat-free diet. + 60 gm. Salad oil daily
Date of exam.	Oct. 7, 1930	Oct. 22, 1930	Oct. 28, 1930
Dry substance:	21 %	24.85%	36.20 %
Ash elements:	17.10 »	11.65 »	8.80 »
Calcium (CaO)	3.25 »	2.30 »	1.60 »
Phosphorus (P ₂ O ₅)	5.10 »	2.40 »	2.05 »
Other elements	8.80 »	6.95 »	5.15 »
Total fat:	12.95 »	56.35 »	59.70 »
Neutral fat	4.30 »	11.50 »	13.45 »
Free fatty acids	5.50 »	41.65 »	44.95 »
Soaps	3.10 »	3.20 »	1.40 »
Other organic substances (rest)	69.95 »	32.00 »	31.50 »

*) Methods of analysis:

Dry substance: Ca. 10.0 gm. with ashed pumice, drying in vacuum, at 98–99°, to constant weight.

Volatile substances: The difference.

Ash: Ca. 10 gm. of fæces ashed over low burner (Argand burner).

Calcium: Weight analysis on solution of ash in nitric acid. (Oxalic acid, ashing and weighing as CaO).

Phosphoric acid: Molybdic acid method.

Free fatty acids: Extraction of dry substance on pumice, powderized, with gasoline (boiling point ca. 50° C). On the dried fat, free fatty acids determined by titration. Difference: Neutral fat.

Soaps: Residue from fat extractions shaking with hydrochloric acid, alcohol ether (Röse Gottlieb method).

**) In No. 1 and No. 3, the total amount of fæces cannot be given, as some portions have been left out on account of admixture with urine.

No. 3. (Fat free diet + 50 gr. butter daily).

Date of exam.	Oct. 4, 1928
<i>Dry substance:</i>	24.25 %
Calcium (CaO)	2 »
<i>Total fat:</i>	60 »
Neutral fat	20 »
Free fatty acids	66 »
Soaps	14 »

No. 4.

	Fat-free diet.	Fat-free diet. + 60 gm. Salad oil daily	Fat-free diet. + 60 gm. butter daily
Date of exam.	Oct. 7, 1930	Oct. 22, 1930	Oct. 28, 1930
Total amount	320 gm.	425 gm.	185 gm.
Dry substance:	16.55 %	19.55 %	21.60 %
<i>Ash elements:</i>	15 »	7.95 »	10.10 »
Calcium (CaO)	2.36 »	0.87 »	1.95 »
Phosphorus (P ₂ O ₅)	3.94 »	1.03 »	2.35 »
Other elements	8.70 »	6.05 »	5.80 »
<i>Total fat:</i>	31.20 »	64.00 »	28.50 »
Neutral fat	6.05 »	18.70 »	13.45 »
Free fatty acids	19.65 »	41.70 »	14.35 »
Soaps	5.50 »	3.60 »	0.70 »
<i>Other organic substances (rest)</i>	53.80 »	28.05 »	61.40 »

No. 5. (Fat-free diet + 50 gr. butter daily).

Date of exam.	Jan. 13, 1928	Feb. 28, 1928
Total amount	450 gm.	940 gm.
Dry substance:	20.3 %	20.8 %
<i>Ash elements:</i>	14.5 »	14.90 »
Calcium (CaO)	5.07 »	4.8 »
Phosphorus (P ₂ O ₅)	3.94 »	4.8 »
Other elements	5.49 »	5.3 »
<i>Total fat:</i>	66.8 »	56.5 »
Neutral fat	20.20 »	26.2 »
Free fatty acids	30.6 »	25.4 »
Soaps	16 »	4.9 »

very wide variations, as it may be also in normal individuals, according to Harrison & Sheldon ⁴⁷.

In 2 cases, No. 1 and 4, where the fat absorption was examined with animal and vegetable fat (butter and salad oil). No. 1 showed the same absorption power for both kinds of fat, whereas No. 4 showed a much greater absorption power for butter. These findings suggest that the insufficiency of the fat digestion is not restricted to the digestion of butter fat but may also apply to the digestion of other fats, as in No. 4 the vegetable fat (salad oil) was utilized to a less degree than was the butter fat. That this deficiency of absorption power may also apply to the fat of woman's milk is demonstrated by experiences in this department, as in 2 cases (with fatal issue) the patients were fed on woman's milk without the stools going down in fat content. Bloch ¹⁰ has observed an aggravation of the fatty diarrhoea under treatment with cod liver oil.

B. Blood Sugar Examination.

Introduction.

In studies on the alimentary hyperglycæmia in patients with sprue, Thaysen ¹¹⁸ and Holst ⁵³ have made the observation that in some of these cases the blood sugar curve is strikingly low.*) Thaysen ¹²⁰ reports that the low blood sugar curve is found after intravenous injection of glucose as well as after ingestion. He thinks, therefore, that the low blood sugar curve can hardly be due to a deficiency in the glucose absorption from the gastro-intestinal tract or to a destruction of glucose in this canal, especially as the ingestion of glucose in these patients produces an increase of the respiratory quotient to about 1; and on a diet particularly rich in carbohydrates the respira-

*) Thaysen & Norgaard ⁵⁰ have defined the »low blood sugar curve» as a curve in which the rise is less than 0.040 % above the fasting value, provided 1) that the blood samples are taken at intervals of 10—15 minutes at the most, 2) that the amount of glucose ingested in adults is ca. 60 gm., and 3) that the Hagedorn-Jensen method is employed for the blood sugar determination.

tory quotient of these patients is also higher than on an ordinary diet of free choice.

Resemblance of the clinical features in sprue and coeliac disease occasioned the blood sugar examinations in some cases of coeliac disease reported in the following.*) One of my cases, No. 5, was given to Thaysen and reported by him at a congress in Wiesbaden, 1928, together with his studies on the blood sugar regulation in sprue. Thaysen has grouped the tropical sprue and the non-tropical sprue together with coeliac disease under the common term: Chronic idiopathic steatorrhoea.

After I had given a preliminary report on some of my examinations on the blood sugar regulation of patients with coeliac disease — read before the Danish Pediatric Society, in 1928 — Mac Lean & Sullivan⁷⁰ (1929) have reported some blood sugar examinations after glucose ingestion in several cases of this disease. These authors gave 1.75 gm. glucose per kg. of body weight and examined the concentration of the blood sugar one and two hours after the glucose ingestion. In this way they found but a slight rise of the blood sugar concentration, amounting at the most to 0.013 %. Similar results were obtained after ingestion of larger doses of glucose, 3—5 gm. per kg. So, as I shall later point out, the results of these authors are suggestive of the same features as are brought out by my examination. But, as mentioned, Mac Lean & Sullivan have taken the blood samples at intervals of 1 hour and this is not enough to give instructive data on the blood sugar curve. (In one case, they took blood samples every 15 minutes for one hour, and in this case they found a blood sugar rise from 0.103 to 0.124 % in 45 minutes. One hour after the glucose ingestion the blood sugar concentration had again come down to 0.101 %). Moreover, for the blood sugar determination these authors have used the Myers-Bailey modification of the Lewis-

*) At a meeting of the Danish Pediatric Society in October, 1927, Dr. C. Friderichsen advanced the idea that it might prove of interest to examine the carbohydrate metabolism of these children for comparison with the findings reported in sprue.

Benedict method — with the sugar determination made on venous blood, which, according to numerous investigators, gives values lower than those obtained with capillary blood.

Own investigations.

The blood sugar regulation was examined after ingestion of glucose in 10 % watery solution — only the large doses were given in 15—20 % solution. All the children took the glucose solution willingly. Their fatty diarrhoea was not aggravated by the ingestion of glucose. For standard dose it was decided to give 1.5 or 2 grams of glucose per kilogram of body weight. In addition, a larger dose of glucose (4—6 gm. per kg.) was employed in some tests. Finally, the blood sugar was examined after subcutaneous injection of adrenalin, and after ingestion of glucose combined with subcutaneous injection of adrenalin. One child (No. 3) was further examined after ingestion of levulose. As a rule, samples of blood were taken at intervals of 5—10 minutes; and, usually the experimental period covered 2½ hours, but occasionally (in case No. 3) a longer time, 3—4 hours (in this case, however, the blood samples were taken at longer intervals in the last part of the examination period).

In turning to mention the results of this glucose tolerance test in each individual case, I shall first point out that *none of these children showed any abnormalities as to fasting blood sugar values*. Their average fasting value was 0.083 %, in variations from 0.070 to 0.097 %.

No. 1 (case record No. 1, p. 128), a boy of 1¾ years, was first examined with 2 gm. glucose per kg. This gave no rise of the blood sugar whatever, apart from what may usually be seen as variations in the fasting values, the fasting value being here 0.084 % and the highest value obtained being 0.093 %. 80 minutes after the glucose ingestion, there was a small fall

of the blood sugar curve to 0.071 %, that is 0.013 % under the fasting level, whereas the rise had been only 0.009 %. The next test, 4 days later, gave a quite similar result. A test with 4 gm. glucose per kg., 11 days after the last test, gave likewise an insignificant rise, amounting only to 0.015 % — i. e., from the fasting value 0.085 % to the maximal value 0.100 % (Fig. 57).

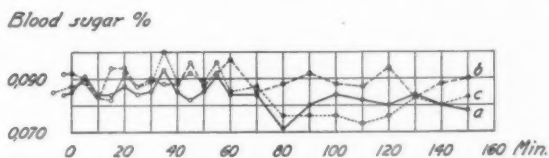


Fig. 57.

Coeliac disease, No. 1. Male. a, June 13, 1930. 2 gm. gluc. per kg.

Age: 1 year and 11 mths. b, » 17, » 2 » » » »

c, » 28, » 4 » » » »

Thus, in none of these tolerance tests did the glucose ingestion (2 or 4 gm. per kg.) produce any rise of the blood sugar worth mention; nor was there any tendency to hypoglycæmia.

Subcutaneous injection of 0.3 mgm. adrenalin gave a somewhat greater rise of the blood sugar concentration; in $\frac{1}{2}$ hour it rose from 0.092 % to 0.116 %, and it stayed at this level for 20 minutes, whereafter there was an abrupt rise to 0.143 % followed by an equally sudden fall — in 5 minutes, the blood sugar concentration was again down to 0.116 %. Then there was a gradual fall in the next $1\frac{1}{2}$ hour, without tendency to Hypoglycæmia. Another test, with ingestion of 2 gm. glucose per kg. and subcutaneous injection of the same dose of adrenalin (0.3 mgm.), gave a slight fall of the blood sugar curve in the first 15 minutes, and then a gradual rise to 0.147 % in the next 40 minutes, followed by a very slow fall for $1\frac{1}{2}$ hour, so that the blood sugar curve had not returned to the level of the fasting value when the test was discontinued, $2\frac{1}{2}$ hours after the glucose ingestion (Fig. 58).

No. 2 (case record No. 2, p. 130), a girl of $2\frac{1}{2}$ years, had on the first test, one month after the admission, 2 gm. glucose

per kg. Like No. 1, she showed no tendency to hyperglycaemia after this dose of glucose. The fasting blood sugar value was 0.087 %; and not till the last part of the examination period — 130 minutes after the glucose ingestion — did there come a slight rise of the blood sugar concentration to 0.107 %,

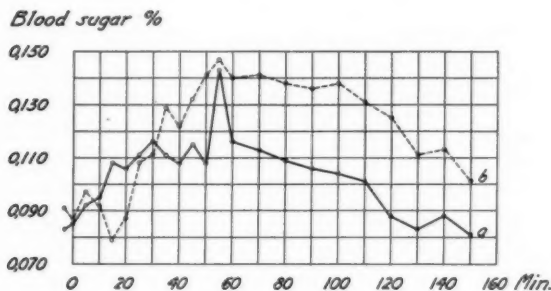


Fig. 58.

Coeliac disease, No. 1. Male. a, June 26, 1930. 0.3 cc. 1 % adrenalin
Age: 1 year and 11 mths. b, » 29, » 0.3 » » »
+ 2 gm. gluc. per kg.

whereafter it again fell off, being 0.097 % at the end of the test. In the next test, 3 days later, with the same dose of glucose there was after 70 minutes a rise of the blood sugar curve to 0.096 % — i. e., a rise of 0.016 % above the fasting value. In the next hour after this rise, the blood sugar curve was falling gradually to the fasting level, 0.074 %, whereafter it again rose a little, to 0.090 % at the end of the test. In other words, in this test the blood sugar curve stayed altogether within the limits of the fasting level. But, in a subsequent test, 4 days later, with 6 gm. glucose per kg., the blood sugar curve showed a rise in the first hour from 0.087 to 0.164 %, whereafter it fell off slowly and gradually, showing a value of 0.112 % at the conclusion of the test 2½ hours after the glucose ingestion (Fig. 59).

The patient was then placed on the aforementioned Kerley diet, and improved considerably; in particular, the stools became formed and less voluminous. A new glucose tolerance

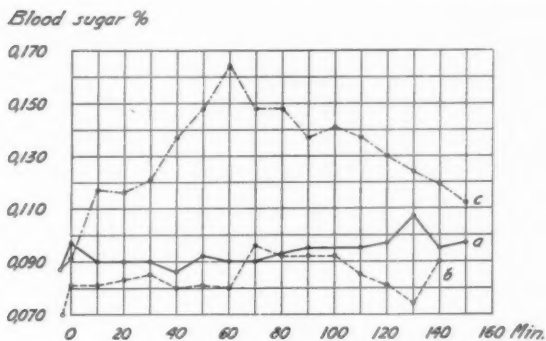


Fig. 59.

Coeliac disease, No. 2. Female. a, July 24, 1929. 2 gm. gluc. per kg.

Age: 2 years and 7 mths. b, » 27, » 2 » » » »

c, » 31, » 6 » » » » »

test, about 4½ months after the first test, with 2 gm. glucose per kg., showed exactly the same features of blood sugar regulation as did the preceding two tests with the same dose of glucose. The tolerance test was again repeated 2½ months later, that is, over ½ year after the first test. At this time, she had improved so much that the stools looked normal, and a rather refractory scurvy had now disappeared. Yet, at this time too, did a tolerance test with 2 gm. of glucose show but a very slight degree of hyperglycaemia. The fasting blood sugar value was 0.095 %. After the glucose ingestion, the blood sugar rose, in ½ hour, only to 0.107 %; and then it fell off to 0.084 %, whereafter it rose once more, reaching again 0.107 % — 90 minutes after the glucose ingestion. After this, the curve went down to the fasting level (Fig. 60).

In this period, a test was made with subcutaneous injection of 0.4 mgm. adrenalin (0.4 cc. of a 1 ‰ solution). This gave a gradual rise of the blood sugar concentration, reaching 0.170 % in 50 minutes, and an equally gradual fall to the fasting level, but no hypoglycaemia. A subsequent test 4 days later, with ingestion of 2 gm. glucose per kg. and subcutaneous injection of 0.4 mgm. adrenalin, showed a rise within 70 mi-

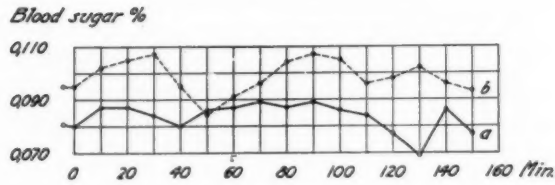


Fig. 60.

Coeliac disease, No. 2. Female. a, Dec. 10, 1929. 2 gm. gluc. per kg.
Age: 2 years and 11 mths. b, March 1, » 2 » » » » »

notes to 0.217 %, and then a fall reaching the lowest value, 0.069 %, at the conclusion of the test, 2½ hours after the glucose ingestion (Fig. 61).

One year later, the patient was again admitted to the hospital for after-examination. She was now 4¼ years. In the meantime she had learned to walk, and mentally she had developed a good deal, though, unquestionably, she was still

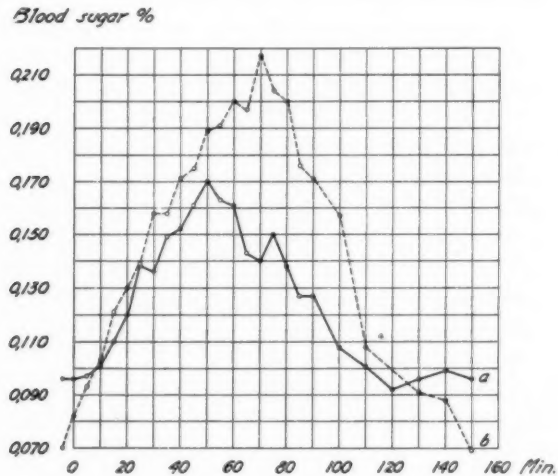


Fig. 61.

Coeliac disease, No. 2. Female. a, March 5, 1930. 0.4 cc. 1 % adrealin
Age: 3 years and 1 mth. b, » 7, » 0.4 » » » »
+ 2 gm. gluc. per kg.

lagging when compared with a normal child of the same age. She had grown $6\frac{1}{2}$ cm. in height, so that she now measured 90 cm. — i. e., the height of a child at the age of 3 years. She weighed 13.250 kg., having gained 3.3 kg., but for her age her weight was still short of ca. 3 kg. Her appearance was still showing evidence of the lesion: flabby muscles, large and distended abdomen. The stools, on the other hand, were no longer voluminous and grey, but normal in their colour and consistency, though somewhat fatty.

She was submitted to 2 glucose tolerance tests one week apart, with 2 gm. glucose per kg.

In the first test, the fasting blood sugar value was 0.094 %. In 40 minutes the blood sugar concentration rose to 0.120 %, and in the next $\frac{1}{2}$ hour it fell off again to the fasting level, where it stayed during the rest of the examination period. In the next test, the blood sugar curve rose in 70 minutes to a maximal value of 0.112 % — i. e., a rise of 0.025 % above the fasting value — and in the next 20 minutes it fell to the fasting level; in the last hour of the examination period, the blood sugar curve showed an after-rise amounting to 0.020 %.

One week later, a tolerance test was made with 6 gm. glucose per kg. This showed a gradual rise of the blood sugar in 50 minutes from the fasting value of 0.095 % to a maximal

Blood sugar %

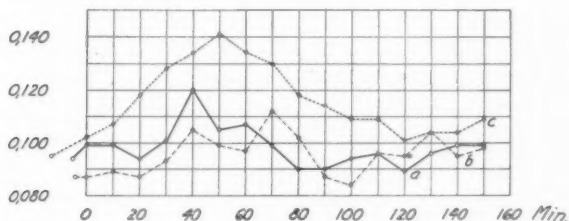


Fig. 62.

Coeliac disease, No. 2. Female. a. April 1, 1931. 2 gm. gluc. per kg.

Age: 4 years and 3 mths. b, " 8, " 2 " " " "

c, " 15, " 6 " " " "

value of 0.141 %, then an equally gradual fall in the next 70 minutes to 0.101 %, and a slight after-rise at the end of the test to 0.109 % (Fig. 62).

No. 3 (case record No. 3, p. 132), was a boy, aged 3 years and 10 months at the beginning of the blood sugar examinations. In the first tolerance test, he had 1.5 gm. glucose per kg. Here the blood sugar curve showed in 40 minutes a gradual rise from the fasting value of 0.071 % to a maximal value of 0.100 %; then it went down at an extremely slow rate, reaching in 140 minutes the lowest value obtained in this test, 0.063 %, at the end of the examination period, 2½ hours after the glucose ingestion. A new test with the same dose was made 12 days later, and this showed even a more insignificant rise of the blood sugar, the fasting value being again 0.071 %, and the maximal value only 0.087 % — 90 minutes after the glucose ingestion. No hypoglycæmic values were obtained in this test. The test with the same dose of glucose was repeated one month later, and it showed again a blood sugar curve of quite the same features. In this test the fasting value was 0.070 %, and the maximal value was 0.090 %, which was reached in 20 minutes after the glucose ingestion; then the curve stayed at the same level the next 50 minutes, whereafter it showed a slight fall, and again a rise in the next 1½ hour. Two weeks later, a new tolerance test was made, this time with 2 gm. glucose per kg. In this test the rise of the blood sugar is a little more pronounced, from 0.077 % to 0.110 % within 75 minutes; in the next 60 minutes there is a slow fall; and, finally, there is a slight after-rise and subsequent fall in the last 45 minutes of the examination period. 10 days later, a test was made with 4 gm. glucose per kg., in 15 % solution. In this test, the blood sugar concentration rose in 30 minutes to 0.147 %, and in the next 2 hours it fell to 0.060 %; then, in the following hour it rose again to the fasting level, showing a value of 0.091 % at the end of the test, 4 hours after the glucose ingestion (Fig. 63). Between the first and the second tests with 1.5 gm. glucose per kg., an examination was made with ingestion of 1.5 gm. glucose per kg. together with sub-

Blood sugar %

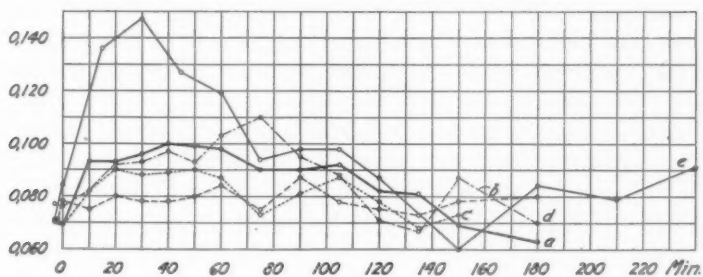


Fig. 63.

Coeliac disease, No. 3. Male. a, Sept. 21, 1928. 1.5 gm. gluc. per kg.

Age: 3 years and 10 mths. b, Oct. 3, " 1.5 " " " "

c, Nov. 11, " 1.5 " " " "

d, " 26, " 2 " " " "

e, Dec. 6, " 4 " " " "

Blood sugar %

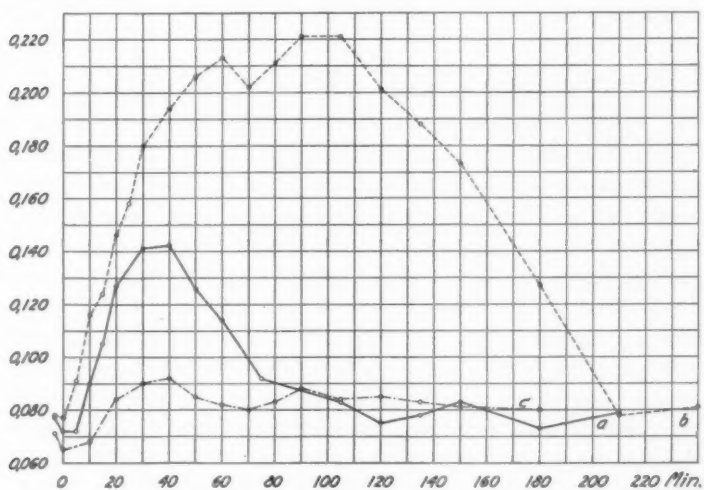


Fig. 64.

Coeliac disease, No. 3. Male. a, Oct. 19, 1928. 0.4 cc. 1 ‰ adrenalin

Age: 3 years and 10 mths. b, Sept. 28, " 0.4 " " " "

+ 1.5 gr. gluc. per kg.

c, Nov. 5, 1.5 gm. levulose per kg.

cutaneous injection of 0.4 cc. 1 ‰ adrenalin. In this test there was an exceedingly high and protracted hyperglycæmia (Fig. 64) beginning in the first hour with a rise of the blood sugar concentration to 0.213 % and followed in the next $\frac{1}{2}$ hour by an additional rise to 0.221 %, whereafter — during the next $2\frac{1}{2}$ hours — the curve fell off to a value of 0.081 ‰. The blood sugar concentration stayed at values above 0.200 % for a period of 70 minutes. There was no sign of hypoglycæmia; still it should be mentioned that after the first $2\frac{1}{2}$ hours the subsequent blood samples were taken at intervals of half an hour, and, of course, it is possible that there might have been a brief period of hypoglycæmia in the last half hour. 3 weeks later a test was made with subcutaneous injection of 0.4 cc. 1 ‰ adrenalin, but without glucose ingestion; this gave a rise of the blood sugar concentration from 0.077 % to 0.142 % in $\frac{1}{2}$ hour, followed by a rather slow fall without hypoglycæmic values, so that the blood sugar curve returned to the fasting level 2 hours after the adrenalin injection. In the next $1\frac{1}{2}$ hour the blood sugar concentration stayed around the same level.

I had an opportunity to examine this patient again $1\frac{1}{2}$ year later, after he had been home during this interval. He had grown but very little since the last admission, so his height was now that of a 4-years-old child, though he was 5 years and 7 months. He did not weigh more than a normal child of 2 years. He was very thin and delicate of frame, but he gave the impression of being remarkably bright, although in somatic respect he was stamped so distinctly by his lesion. The stools were normal in amount, form and consistency. Glucose tolerance test, this time with 2 gm. glucose per kg., showed again but a slight rise of the blood sugar, yet a little greater than in the tests $1\frac{1}{2}$ year before, the rise being now from a fasting value of 0.079 % to the maximal value, 0.116 %, in 40 minutes. Then there comes a gradual fall to 0.069 %, 90 minutes after the glucose ingestion, and this is followed by a new rise to 0.109 % at 130 min. with a slow fall in the last 20 minutes of the examination period. Ingestion of 4 gm. glucose

per kg. gave a rise from 0.095 % to 0.137 %, within 20 minutes, and a gradual fall, so that the curve reaches the initial level in the next 50 minutes. Subcutaneous injection of 0.4 cc. 1 ‰ adrenalin gave similar results as in the preceding tests: a gradual rise to 0.150 % within 1 hour, and an equally gradual fall, with the lowest value, 0.068 %, at the end of the test — $2\frac{1}{2}$ hours after the glucose ingestion (Fig. 65).

Blood sugar %

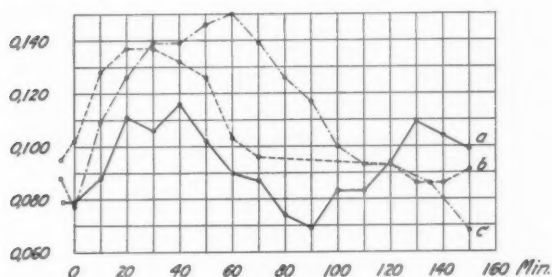


Fig. 65.

Coeliac disease, No. 3. Male. a, May 16. 1930. 2 gm. glucose per kg.

Age 5 years and 6 mths. b, May 20. 1930. 4 gm. glucose per kg.

c, » 23, » 0.4 cc. 1 ‰ adrenalin.

No. 4 (case record No. 4, p. 134). This was a girl, aged 5 years and 7 months, whose illness had been recognized about a year before I had the occasion to examine her. Like the other children, her habitus was stamped distinctly by her illness. The first two glucose tolerance tests, at 4 days' interval, were made with ingestion of 1.5 gm. glucose per kg. In the first test, the blood sugar concentration rose in 55 minutes from 0.084 to 0.102 %, and in the next $1\frac{1}{2}$ hour the blood sugar curve fluctuated between these two values with some small rises and falls (Fig. 66). The next test, 3 days later, showed quite similar features in the blood sugar curve. Here the blood sugar concentration rose in 1 hour from 0.085 % to 0.108 %. One week later, a test with 4 gm. glucose per kg. (in 20 % solution) had to be discontinued after 1 hour, because the patient

at this time regurgitated a large amount of fluid. She did not like to take the concentrated glucose solution, so no attempt was made to continue the test. During the one hour in which blood samples were taken, the blood sugar concentration only rose from 0.092 to 0.112 %, and thus this large dose of glucose did not give any tendency to hyperglycæmia, either. But, of course, the nausea may have had something to do with this negative outcome.

A subsequent test, 4 days later, with subcutaneous injection of 0.4 cc. 1 % adrenalin showed a rise of the blood sugar concentration from 0.076 to 0.186 % within 40 minutes, and then a gradual fall to 0.068 % at the end of the test, 2½ hours after the glucose ingestion. 3 days later, a test was made with ingestion of 1.5 gm. glucose per kg. — subcutaneous injection

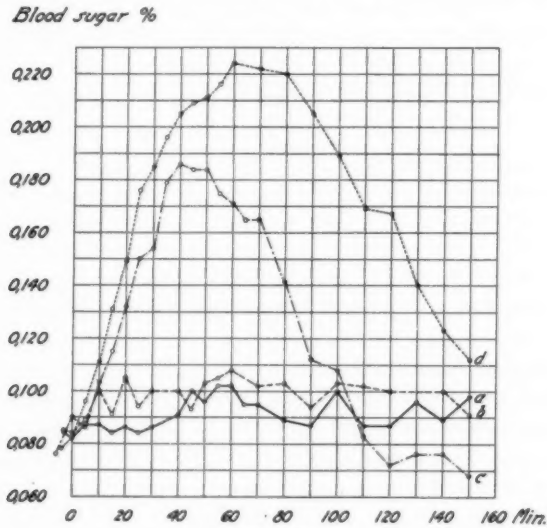


Fig. 66.

Coeliac disease, No. 4. Female. a, Sept. 13, 1930. 1.5 gm. gluc. per kg.
 Age: 5 years and 7 mths. b, » 16, » 1.5 » » » »
 c, Oct. 7, » 0.4 cc. 1 % adrenalin
 d, » 9, » 0.4 » » »
 + 1.5 gm. gluc. per kg.

of 0.4 cc. 1 %₁₀₀ adrenalin. Here the blood sugar concentration rose in 1 hour to 0.224 %, and then it fell off gradually. At the end of the test — after 2½ hours — the blood sugar curve had fallen to a value of 0.112 %. So the hyperglycaemia was not over yet. In this test, the blood sugar concentration stayed on values above 0.200 for about 1 hour (Fig. 66).

No. 5, (case record No. 5, p. 136), the oldest of these patients, was a girl, almost 11 years old, who had been suffering from coeliac disease for several years. Tolerance test with 1 gm. glucose per kg. showed a rise of the blood sugar from 0.070 % at the beginning of the test to a maximal value of 0.090 % at the end of the test. Thus, in this test, the blood sugar curve resembles the curves that may be obtained on examination of fasting individuals (cf. examinations of blood sugar in fasting, p. 39). A test with 2 gm. glucose per kg. showed a very slight rise in 20 minutes, from 0.097 to 0.109 %, and then a very slow and protracted fall, reaching the lowest value, 0.082 %, in 130 minutes after the glucose ingestion (Fig. 67). Unfortunately, there was no opportunity to make any further tests on this patient.

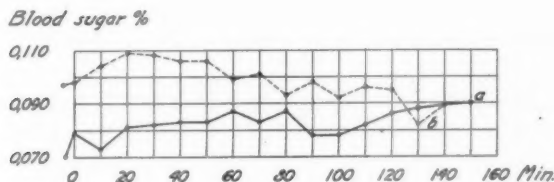


Fig. 67.

Coeliac disease, No. 5. Female. a, Feb. 22, 1928. 1 gm. gluc. per kg.
Age: 10 years and 9 mths. b, " 26, " 2 " " " "

Table 16 gives in abstract the most important features of the blood sugar curve obtained in the various tests on these 5 patients.

As the general result of these blood sugar examinations it is found that *in patients with coeliac disease there is a tendency to an exceedingly slight hyperglycaemia after ingestion*

Table 16.
Blood Sugar Examinations in Coeliac Disease.

Pt. No. Age Date of Exam.	Test Dose*	Maximal Value ‰	Time of Max. Val. min.	Rise of Blood sugar ‰	Duration of Hyper- glycæ- mia†min.
No. 1					
1 y. 11 m. 6-13-30	2 gm. gluc.	0.093	35	0.009	
6-17-30	2 gm. gluc.	0.097	60	0.005	
6-28-30	4 gm. gluc.	0.100	35	0.015	
6-26-30	0.3 cc. adrenalin	0.143	55	0.060	120
6-29-30	0.3 cc. adrenalin + 2 gm. gluc.	0.147	55	0.056	> 150
No. 2					
2 y. 11 m. 7-24-29	2 gm. gluc.	0.107	130	0.020	
7-27-29	2 gm. gluc.	0.096	70	0.016	
12-16-29	2 gm. gluc.	0.089	70	0.008	
1- 3-30	2 gm. gluc.	0.107	30	0.012	
7-31-29	6 gm. gluc.	0.164	60	0.077	> 150
3- 5-30	0.4 cc. adrenalin	0.170	50	0.074	120
3- 7-30	0.4 cc. adrenalin + 2 gm. gluc.	0.217	70	0.147	130

*) Glucose and levulose doses are grams per kilogram of body weight, given by mouth. Adrenalin is a 1 ‰ solution, given by subcutaneous injection.

†) In several of the tests this value has been left out, because here the rise of the blood sugar concentration has really been too small to warrant the term hyperglycæmia.

Table 16 (cont.).

Pt. No. Age. Date of Exam.	Test Dose	Maximal Value %	Time of Max. Val. min.	Rise of Blood Sugar %	Duration of Hyper- glycæ- mia min.
No. 3					
3 y. 10 m. 9-21-28	1.5 gm. gluc.	0.100	40	0.029	
10-13-28	1.5 gm. gluc.	0.084	60	0.013	
11-11-28	1.5 gm. gluc.	0.090	20	0.020	
11-26-28	2 gm. gluc.	0.110	75	0.033	
12-6-28	4 gm. gluc.	0.147	30	0.077	75
11-5-28	1.5 gm. levul.	0.092	40	0.021	
9-28-28	0.4 cc. adrenalin + 1.5 gm. gluc.	0.221	90	0.143	210
10-19-28	0.4 cc. adrenalin	0.142	40	0.065	75
5-16-30	2 gm. gluc.	0.116	40	0.037	60
5-20-30	4 gm. gluc.	0.137	20	0.042	70
5-23-30	0.4 cc. adrenalin	0.150	60	0.062	110
No. 4					
5 y. 7 m. 9-13-30	1.5 gm. gluc.	0.102	55	0.018	
9-16-30	1.5 gm. gluc.	0.108	60	0.023	
9-23-30	4 gm. gluc.	0.112	(in 60 min., when test interrupted by vomiting)		
10-7-30	0.4 cc. adrenalin	0.186	40	0.110	110
10-9-30	0.4 cc. adrenalin + 1.5 gm. gluc.	0.224	60	0.146	> 150
No. 5					
10 y. 9 m. 2-22-28	1 gm. gluc.	0.090	150	0.020	
2-26-28	2 gm. gluc.	0.109	20	0.012	

of glucose in doses of 1—2 gm. glucose per kg. of body weight. This peculiarity of the blood sugar regulation in these children appears remarkably constant in tests at different times, at intervals even of months and years, and even when these patients are examined in periods of definite improvement (especially with regard to the amount and consistency of the stools). A low blood sugar curve after ingestion of glucose in the doses mentioned is therefore to be regarded as a sign of diagnostic importance in coeliac disease.

The question is then: Is the low blood sugar curve attributable to a defective absorption of glucose from the intestinal tract, or to a deficiency of glycogen in the organism, or, perhaps, to an excessive production of insulin?

Against the probability of a defective absorption goes the fact that — as shown in No. 2 and 3 — a rather considerable rise of the blood sugar may be obtained by ingestion of larger amounts of glucose (4—6 gm. per kg.). Further, the absorption of the glucose is also evident from the fact that glucose ingestion + adrenalin injection gives a far greater and more protracted hyperglycaemia than the sum of the blood sugar rises after glucose alone and adrenalin alone. The same is also suggested by the findings in a single examination of the respiratory quotient*) on No. 5, who showed an increase of this quotient after ingestion of carbohydrates.

The blood sugar rise after injection of adrenalin goes against a deficiency of glycogen in the organism, at least to any marked degree. The blood sugar values obtained in such tests are similar to those obtained in normal adults (Brems¹²) and in normal infants (Beumer & Schäfer⁷).**)

In one case (No. 3) the blood sugar regulation was examin-

*) Carried out in the laboratory of Dr. Hagedorn.

**) In one case of *mb. Addisonii* reported by Wadi^{12a}, intravenous injection of 0.2 mgm. of adrenalin did not give any increase of the blood sugar values. On the contrary, for instance, 8 minutes after the injection the blood sugar value is 0.051; and $\frac{1}{2}$ hour later it is 0.043. At the same time there were signs of hypoglycaemic shock.

ed after ingestion of 1.5 gm. levulose per kg. of body weight. The blood sugar concentration rose from 0.071 to 0.092 %, which comes within the normal limits in levulose tests. This does also suggest that the liver function is not impaired. In this connection, I may refer to M. Brown¹⁴, who in her investigations on normal children found the blood sugar concentration after levulose ingestion varying from a fall of 0.010 % to a rise of 0.28 %; she considers a rise above 0.030 % to be a sign of liver disease.

The possibility of an excessive production of insulin is refuted by the fact that these patients show no particular tendency to hypoglycæmia. The fact that they show normal fasting values may perhaps be interpreted as suggestive of this point, too.

To me it seems probable that the slight alimentary hyperglycæmia in coeliac disease can not be due primarily to an abnormality of the carbohydrate metabolism, but that we here are dealing with a secondary result of an abnormality in the fat metabolism. The low blood sugar curve may then be due to an unusually rapid assimilation of the glucose absorbed.

There can be no doubt that in coeliac disease we are really dealing with a pathological change in the behaviour of the organism to fat. What is actually the matter, we know as yet but very little. The enormous output of fat with the fæces is regarded by most authors as due to defective absorption of the fat ingested. Yet, some investigations have been reported that are suggestive of another causality. Thus, as mentioned before, Moncrief & Payne⁸⁵ find that after fatty meals the fat content of the blood is greater than normal; and they think, therefore, that the large amount of fat in the fæces is not due to a defective absorption of ingested fat, but to an increased elimination of fat from the blood.

This view is also supported by the aforementioned investigations of Miller, showing that considerable amounts of fat are eliminated with the fæces even on a fat-free diet. The same is found on examination of the fæces from my patients No. 1 and 4 (see p. 106 and 107). Here, the fat-free diet notwith-

standing, the fat content of the faeces is respectively ca. 13 and 31 % of the dry substance.

The possibility is not excluded, I think, that in coeliac disease we are dealing with a disturbance of the fat metabolism, manifesting itself by inability of the patients to utilize fat in normal way. As a set-off, their carbohydrate metabolism is the more active. It does not seem unreasonable in this lesion to think of a hormone insufficiency and to see a parallel with diabetes mellitus. At any rate, it seems to me, this view constitutes a fairly serviceable working hypothesis for further studies on the interaction of the fat and the carbohydrate metabolisms.

To see whether the peculiar low blood sugar curve may be found also in other diseases of children where the stools are voluminous and fatty I have examined some infants suffering from chronic dyspepsia, such stools being absent in greater children under my observation.

Table 17.

Glucose Tolerance Tests in Dyspepsia.

(5 children, from 2 months to 1 year old; 9 tests with 2 gm. glucose per kg.).

	Average	Variations
Fasting values % ₀	0.077	0.063—0.092
Maximal values % ₀	0.186	0.155—0.211
Rise of blood sugar % ₀	0.109	0.081—0.133
Time of maximal value (min.)	46	20—100
Duration of hyperglycæmia (min) ..	116	90—140

This examination comprises 5 children in the first year of life. In none of these cases did the alimentary hyperglycæmia differ from what is found in normal children of the same age. The fasting values varied from 0.063 to 0.092 %, with an average of 0.077 %. The maximal values varied from 0.155 to 0.211 %, with an average of 0.186 %. The maximal values were reached in $\frac{1}{2}$ —1 hour; and the hyperglycæmia was over in less than $2\frac{1}{2}$ hours.

Case-records of Coeliac Disease.

No. 1. — Boy Reg. No. 22/1931. Born, July 31, 1928.

1 $\frac{3}{4}$ years.

Adm. May 21, 1930.

Disch. Jan. 10, 1931.

Blood sugar exam.: June 13, 17, 26, 28 and 29, 1930.

The patient is the son of a country mechanic. He is the second of 3 children, and the 2 others are well. He was born at full term, by natural delivery; he was sucking the first 4 months, whereafter he had increasing milk mixtures. Since the age of 1 year, he has had ordinary children's diet.

When 6 months old, the patient had a severe attack of bronchitis. 2 weeks before the admission, he began to have frequent vomiting; shortly after, the stools became slimy, thin and stinking. No elevation of temperature. Admission diagnosis: *Tabes meseraica*.

On admission: A small child (73.5 cm.), thin, with rather marked signs of rickets; ca. 4 kg. under normal weight. Abdomen sunken, without tenderness; no swelling of organs. Turgor lowered; slight swelling of cervical and inguinal glands. *Pirquet* \div . *Hæmoglobin*: 84 %. *Urine*: No abnormalities.

Stools: The first days after adm., several stools a day, foetid and slimy. After 3 days' diet, the stools were homogenous, non-stinking and not slimy. Some time later, after the patient had been placed on ordinary diet, the stools became again voluminous, slimy, stinking and somewhat fatty. At times they were more firm and pasty, but yet very foul and voluminous; 2–4 stools a day.

The patient lost all his appetite and was very weak. 2 test meals (barley water) showed complete achylia. At this time some blood sugar examinations were made with ingestion of glucose. This had no effect on the stools.

One month after adm. the patient had lost 200 gm. in weight. His habitus was apathetic; the muscles were flabby, the buttocks markedly flattened and wrinkled. The skin was pale, with spots of pig-

mentation on the neck, back and cheeks; no pigmentation of the mucous membrane of the cheeks. Rather marked lanugo on the cheeks and neck, lips and chin, and along the midline of the back.

Auscultation of the lungs and heart showed no abnormalities.

Abdomen: No enlargement of the liver and spleen; no tenderness on palpation. In contrast with the flaccid and sunken abdomen on adm., it is now disproportionately large for the little and thin body. The percussion note was tympanitic over the entire abdomen.

Extremities thin. Teeth, $\frac{a}{s}$, showing a marked degree of caries. Electrical irritability increased (C. O. C. 2).

Blood pressure: Systolic, 75 mm. (palpation). 2 months later, 90/40 (auscultation).

The patient was now placed on a diet consisting of sodium caseinate and barley gruel (see p. 102), fruit — especially bananas and strawberries — puree of apples, mashed potatoes, spinach, puree of carrots, lemonade, and zwiebacks. *No milk*. As the hæmoglobin had gone down and stayed between 60 and 70 %, iron was given (Ferrum reductum).

The patient now began to straighten up from his condition of apathy. The turgor was better, and the muscles less flabby. But the stools kept on being voluminous, foetid and fatty. In the next month he gained 800 gm. in weight.

Test meal (barley water) after 3 months' stay in the hospital showed normal values; and so did 4 subsequent test meals one month apart.

Fæces analysis: see p. 106.

5 months after adm.: With the above-mentioned diet, the stools as a rule were formed, not abnormally large, non-stinking and coloured by iron. The hæmoglobin percentage was now 90. In the past 5 months (while in the hosp.) he had grown but 0.5 cm., but he had gained 1.5 kg. in weight. Yet he was still thin; the turgor was bad, the muscles flabby and the buttocks atrophic. Conspicuous lanugo and pigmentation as before. Marked tendency to sweating, both night and day. The abdomen was still distended and large in contrast with the thin extremities. No enlargement of the organs.

X-ray exam.: Rachitic changes in the bones, but no retardation in the development of the carpal bones.

Temperature: Apart from a rise of the temperature in connection with a cold (twice) it has been normal all the time.

7 months after adm., when the patient was discharged, he had improved considerably, but most in mental respect. As a rule, he was jolly, bright and active, in contrast with his former condition of

apathy; and he had commenced to talk and run around in his coop. Somatically, however, his condition was rather unchanged.

On adm., May 21, 1930:	Weight	8.100 kg.	Height	73½ cm.
On disch., Jan. 10, 1931:	»	10.500 »	»	76½ »
	+	2.400 »	+	3 »

No. 2. — Girl. Reg. No. 194/1931. Born, Jan. 5, 1927.

Adm. June 20, 1929. 2½ years.

Disch. March 8, 1930.

Readm. March 26, 1931. 4¼ years.

Disch. April 16, 1931.

Blood sugar exam.: July 24, 27 and 31, Dec. 16, 1929,

March 1, 5 and 7, 1930,

April 1, 8 and 15, 1931.

The patient is the daughter of an unmarried housekeeper, of Copenhagen. Family history negative. She was born at full term by natural delivery; she was sucking the first 3 weeks, whereafter she was fed on milk mixtures. She was well till she was 10 months, when she had rickets. For this she was admitted to this department on May 21, 1928, where she stayed till June 14, 1928.

Clinical diagnosis (June, 1928): Tuberculosis latens. Rachitis.

Anæmia.

The stools were frequently loose, slimy, but not particularly voluminous or fatty. The abdomen was large and somewhat distended, but without tenderness even on very deep palpation; and no enlargement of the organs or intumescence could be made out. *Pirquet* +. *Hæmoglobin*: 74–80 %.

She improved a great deal while in the hospital, and in a sea-shore sanatorium, to which she was transferred and where she stayed 9 months. Shortly after her return home, she was falling off again; her appetite was very poor, and she could hardly stand on her feet; she was altogether unable to walk. At the same time, the stools became loose and greenish, stinking; 2–3 bowel movements a day. After this had been going on about 4 months, she was admitted to this department under the diagnosis: *Dyspepsia chronica*.

On admission: Small child, thin, with flabby muscles; weight 8.600 kg., i. e., hardly the weight of a normal child at the age of 1 year. Height 81 cm. Good colour of skin, but pale mucous membranes. *Hæmoglobin*: 65 %. The skin was dry, and the turgor lowered. The abdomen was somewhat distended. The patient was apathetic and whimpering; she refused to talk, and looked as if suffering.

There were marked signs of rickets, and conspicuous swelling of the gums with tendency to bleeding. There were no pigmentations. Rather marked lanugo.

Stools: 2—3 bowel movements a day, voluminous, loose and putrid.

Her diet was first composed of milk mixtures; later she had fluid diet and crackers, beside lemonade. After 1 month she was on a diet consisting in casein and barley gruel (see p. 102), fruit, puree of carrots, mashed potatoes, spinach, and bananas. *No milk.* At this time she was still very weak, with flabby muscles and atrophic buttocks. She could stand up only when supported. The abdomen was large, in contrast with the thin body, but without any tenderness or intumescence. When the patient had been on this diet for some time, the stools became formed, less voluminous and less stinking. There was no change in the weight the first 3 months. After some time, the casein-barley gruel did no longer agree with the patient; it gave her nausea, so protein-milk was given instead. In this period the stools again became loose and greasy.

A month later, a new attempt was made with casein-barley gruel, and this time she took it with relish. Once more the stools became formed and non-stinking, and the bowels moved but once a day. But, in spite of an abundant supply of fresh fruit, her gums kept on being swollen and bluish in colour; there still remained some tenderness of the bones, and hæmaturia was observed a few times.

Not till 4 months after her admission did the scorbutic symptoms subside, and the patient began to be able to get up and stand on her feet. Now her apathy left her, and she began to talk in sentences.

In the first two months, Ewald test meal showed achylia. A couple of months later, the test meal showed normal values of acidity; but achylia was again present in the next two months. Finally, during her last two months in the hospital the gastric analysis showed normal conditions.

At the discharge, after 9 months in the hospital, the child was over 3 years old. She weighed only 10.550 kg.; she had grown $2\frac{1}{2}$ cm. since her admittance, so she now measured 83.5 cm. in height. She was still looking poorly, with flabby muscles, sluggish turgor, flattened buttocks, distended abdomen, and thin and dry hair. No pigmentations. *Hæmoglobin* 70 %. The stools were formed and homogenous, not fatty, normal in colour, smelling markedly sour.

On adm. June 20, 1929: Weight 8.600 kg. Height 81.0 cm.

On disch., March 8, 1930. " 10.550 " " 83.5 "

 + 1.950 " + 2.5 "

One year later the patient was readmitted for after-examination and regulation of diet.

During the past year she had gained 3.3 kg. in weight, and she had grown 6.5 cm. Thus she had the height of a normal child of 3 years and the weight of a child aged $2\frac{1}{2}$ years. She still has some conspicuous marks of the old lesion: large and distended abdomen, flabby and poor muscles. As before, she showed signs of rickets in form of epiphyseal swelling and Harrison's groove. The skin was pale but otherwise normal, without pigmentation. There was no abnormal hairiness, apart from some lanugo on the upper part of the back. The tongue looked normal. *Hæmoglobin* 64 %. Blood pressure 80/60. No sign of tetany.

Stools. In the past year the bowel movements had usually been regular, daily and spontaneous, with formed stools of normal colour. At times, however, there had been constipation, and at other times periods of diarrhoea with voluminous, greyish and foetid stools. Here in the hospital, the bowels were regular, moving daily, with stools of normal colour and consistency but a little greasy.

Mentally the child was fairly quick, not irritable, but undoubtedly somewhat behind normal children of the same age.

Here in the hospital she was on an ordinary diet with milk, and it agreed with her.

Thus her condition has certainly improved, though the lesion still manifests its presence now and then.

No. 3. — Boy. Reg. No. 283/1930. Born, Nov. 21, 1924.

Adm. June 11, 1928. 3 $\frac{1}{2}$ years.

Disch. May 18, 1929.

Readm. May 14, 1930. 5 $\frac{1}{2}$ years.

Disch. May 30, 1930.

Blood sugar exam.: Sept. 21, Oct. 3 and 19, Nov. 5, 11 and 26, 1928.

May 16, 20 and 23, 1930.

The patient is the son of a country minister. Family history negative.

The patient was born at full term, by natural delivery. He had mother's milk the first three months, then milk mixtures, and later ordinary diet (always including at least 500 cc. milk daily). He was able to walk when 18 months old. Whooping-cough at the age of 2 years.

The *present illness* began gradually when the patient was $2\frac{1}{2}$ years old, with bowel derangement for periods of 2—3 days, when the stools were thin, slimy and putrid. In the intervals between these

periods the stools were normal. The child was losing weight and gradually getting poor.

On admission, when $3\frac{1}{2}$ years old, he was little for his age, pale and thin, with poor turgor and flabby muscles. No signs of rickets. Height 87 cm., weight 11.3 kg. — i. e., the height of a normal child aged $2\frac{1}{2}$ years and the weight a little less than that of normal child at the age of 2 years. In marked contrast with the thin extremities, the abdomen was large and distended. No enlargement of organs; no tenderness on palpation. No signs of tetany. *Pirquet* \div . *Hæmoglobin* 71 %. The stools were loose, very voluminous, greyish-white in colour and stinking.

He was now placed on a *milk-free diet*, on which he improved somewhat. But as soon as a little milk was added to the diet, his condition got worse again. Now he was put on a diet consisting of casein-barley gruel (see p. 102), bananas, purees of vegetables, scraped broiled meat, but no butter or fat; and he began again to improve. Under this treatment the stools were formed, normal in colour, less voluminous and less stinking. A single relapse was brought on by a meal consisting of 60 gm. bread and 350 cc. milk, which was given for the sake of blood sugar examination. For several days after this meal the stools were greyish in colour and voluminous, accompanied by vomiting and colic. *Ewald test meal* showed normal values in the various stages of the lesion. Repeated examinations of the stools did never show the presence of parasites. *Fæces analysis*, see p. 107. Urine: No abnormalities. *Hæmoglobin* rising from 71 % (on June 12, 1928) to 100 % (on April 19, 1929).

The child was discharged after 11 months in the hospital, on a diet consisting of butter milk gruel, fruit soups, mashed potatoes, rye bread, plenty of fruit, especially bananas, 25 gm. butter, fish balls, meat balls, one egg, crackers, and zwieback. No milk.

After his discharge, the child was lively and bright, having usually a good appetite. Now and then a period of 2–3 days with vomiting, followed by pains in the abdomen and thin stools. As a rule, the stools were light in colour, thin, slimy and stinking; two bowel movements a day. While at home, he was said to have had 5–6 attacks of »cramps with spasms of the lower extremities«; these attacks were independent of the season and of the condition of the stools.

Examination on readmission, May 14, 1930:

The patient is now $5\frac{1}{2}$ years old; he still is little and thin. Since the last admission he has grown $3\frac{1}{2}$ cm., so that he now measures 95 cm. — i. e., the height of a normal child at the age of 4 years. When discharged, a year ago, he weighed 13.100 kg.; and now he weighs but 12.200 kg. Thus, in the past year he has lost 900 gm. in

weight, and now he does not weigh more than a normal child of 2 years. He is very thin and spare of frame, with poor and flabby muscles, but otherwise he looks surprisingly bright and lively. The turgor of the skin is lowered but little; pigmentations are present on the face and hands, also in the axillæ. Besides there are some spots of pigmentation on the lower part of the chest, and the abdomen, and on the back. No pigmentation of the mucous membranes of the mouth. There is a marked degree of lordosis. The abdomen is very large and distended, measuring 48 cm. in circumference. The buttocks are flattened. The milk teeth show a marked degree of caries. His mental development appears fairly normal; he recognizes the personnel of the hospital. *The stools* are normal in form, amount and consistency. One day they are loose, very abundant, foetid and foamy, but the next day they are normal again. *Pirquet* still \div . *Ewald test meal*: Normal findings. *Electrical exam.*: Normal irritability (C. O. C. > 5). Also examination of the blood shows normal conditions as to number and characters of red and white corpuscles. *Hæmoglobin* 84 %. *Temperature* normal throughout his stay in the hospital. He is placed on ordinary diet, \div milk + 500 cc. buttermilk gruel, plenty of fruit. This diet agrees well with him.

On adm., May 14, 1930: Weight 12.200 kg. Height 95 cm.

On disch., » 30, 1930: » 13.000 »
+ 800 gm.

No. 4. — Girl. Reg. No. 530/1930. Born Febr. 22, 1925.

Adm. Oct. 29, 1929.

4 years 8 mths.

Disch Dec. 8, 1929.

Readm. Sept. 11, 1930.

5½ years.

Disch. Nov. 7, 1930.

Blood sugar exam.: Sept. 13, 16, and 23, Oct. 7 and 9, 1930.

The patient is the daughter of a minister, of Copenhagen. Family history negative.

The patient is No. 2 out of 3 children; she was born at full term by natural delivery. She was well till she was a couple of years, when she had two attacks of influenza. She has since been thriving poorly, having no appetite. The bowel movements have been daily and spontaneous, but the stools have been very large and loose, foetid and greasy. There has never been diarrhoea. Sometimes the child has complained of abdominal pains.

On admission, at the age of nearly 4¾ years: Child measures 105 cm. in height, which is rather more than normal for her age; but she weighs only 16 kg. There are slight rachitic deformities of the

thorax. The abdomen is strikingly large in proportion to the rather thin extremities. The skin is normal. Mentality perfectly normal. *Hæmoglobin* 91 %.

During her *first stay* in the hospital, the stools were as described above, and she was treated with a diet consisting of casein-barley gruel (see p. 102), mashed potatoes, puree of carrots, fruit, crackers, lean meat, but *no milk*. Under this treatment she improved. The stools became formed, not particularly greasy or stinking.

After her discharge, she kept on being poor, with frequent attacks of diarrhoea and vomiting, but the diet was not kept either.

Exam. on readmission: The patient is now 5½ years old, rather tall for her age (111 cm.) but thin, with poorly developed muscles. She has grown 6 cm. since last, but weighs only 17.100 kg., which is ca. 4 kg. under the normal weight. The abdomen is large and distended, no tenderness on palpation; no enlargement of organs. The buttocks are not atrophic. Lanugo is present on the cheeks and the extensor surfaces of the arms and legs. The child is very sunburned. (Later, when the sunburn has disappeared, there is no particular pigmentation). The teeth show a marked degree of caries. *Hæmoglobin* 95 %.

X-ray exam.: No signs of rickets.

Stools (the first couple of days): Large, greyish, greasy and stinking, without mucus.

The child was placed on a diet consisting of casein-barley gruel, purees of vegetables, lemonade and fruit, broiled, scraped meat, scarce butter, but *no milk*. Under this treatment the stools became fairly normal, the bowels moving once or twice a day. After 2 months' stay in the hospital, she had gained 900 gm. in weight. For about 1 week she had ordinary diet (without milk), as gradually she objected to take casein-barley gruel. On this diet the stools stayed fairly normal, being strikingly large only now and then. Mentally she was bright and normal. No particular change in the findings on physical exam., excepting that the abdomen seemed rather less distended.

Ewald test meal, Sept. 11 and Nov. 4: Normal findings.

Blood pressure, Oct. 8: 95—60 (auscultation).

Fæces analysis, see p. 107.

On adm., Sept. 11, 1930: Weight 17.100 kg. Height 111 cm.

On disch., Nov. 7, 1930: » 18.000 »
 + 900 gm.

No. 5. — Girl. Reg. No. 226/1928. Born May 2, 1917.

Adm. several times, last adm. April 27, 1928. 11 years.

Disch. May 11, 1928.

Blood sugar exam.: Febr. 22 and 26, 1928.

The patient is the daughter of a well-to-do farmer. One sister died of abdominal tuberculosis. Otherwise, the family history is negative. The patient is the youngest of 11 children, born at full term by natural delivery. The child was bottle-fed on account of hypogalactia in the mother. She was well and thriving till the age of 18 months, when she had a severe attack of »Spanish flue«, complicated with pneumonia and enteritis. After staying in bed 2 months, she was no longer able to stand on her feet, though previously she had been running around. The stools kept on being putrid and thin, after the actual condition of enteritis was over, but they did not contain any blood. Gradually the abdomen was very distended. In *March 1921*, when she was about 4 years old, she was *admitted* to this department. She was little and thin, with poor turgor and flabby muscles, but no paresis. The reflexes were normal. She was unable to walk or to stand without support. There were some signs of rickets. The abdomen was large and distended, without tenderness or intumescence. The right cornea was the site of a pea-sized leucoma. During her stay in the hospital there developed a tenderness of the bones, hæmorrhages into the skin and hæmaturia. *X-ray exam.* showed rachitic changes and signs of scurvy. *Blood examination* (2 times) showed simple anæmia. *Pirquet* ÷. *Wassermann test* ÷. The stools were persistently greyish-white, greasy and slimy, spongy and very foetid, without blood or eggs of parasites. *Ewald test meal* (2 times): Normal findings.

Various forms of dietary treatment were ineffective with regard to the stools. The scurvy, on the other hand, subsided rapidly on a high vitamin diet. At that time, the clinical diagnosis was: *Insufficiencia pancreatis*.

At her *discharge, after 3 months in the hospital*, there was no marked improvement of her condition. At home, however, she was gradually improving, and her health was fairly good during the next 6 years, apart from occasional periods of bowel derangement. She was still lagging considerably in growth. At the age of 10 years, she began again to fall off in health; she was losing appetite, and going down in weight; and she had diarrhoea, with 5–6 stools daily. The stools were loose, whitish in colour, and foetid. No fever.

She was *admitted on Dec. 10, 1927* for *tabes mesaraica* and *avitaminosis*. On admission she measured 118 cm. in height and weighed 19 kg. — i. e., she was 10–12 cm. below the normal height for her age and ca. 10 kg. below the normal weight. Mentally she was nor-

mal, though a little cross; but she was very intelligent for her age. She was extremely emaciated with very poor muscles, dry skin, lowered turgor, numerous petechial hæmorrhages and ecchymoses. The hands were in tetany position, but there was no facialis phenomenon. There was in addition an eye lesion that proved to be xerophthalmia. The abdomen was large and distended, but without any sign of ascites; no enlargement of the organs; no intumescence; no tenderness. *Pirquet* ÷. *Hæmoglobin* 67 %. The bowels moved 5—6 times a day, sometimes even more. The stools were stinking, whitish in colour; when left standing a fatty layer would appear on top.

On account of her eye lesion she was treated with injections of vitamin A, and she responded well to this treatment. In addition, she had plenty of fruit and vegetables. Under this treatment the xerosis and scurvy disappeared. The stools became formed and less frequent, but still voluminous and light in colour. She gained 3 kg. in weight. There was a brief relapse of the eye lesion, but this subsided on injection of vitamin A.

After her *discharge*, Jan. 27, 1928, there was an exacerbation of her illness, at home.

She was *readmitted* on Febr. 20, 1928. The symptoms were the same as before, though now the stools were foamy, fermenting and watery. *Fæces analysis*, see p. 107. *Hæmoglobin* 68 %. Blood picture normal.

She was *discharged* on March 14, 1928, by request of the parents.

Readmitted April 27, 1928, and again
discharged on May 11, 1928.

Her condition kept on being very poor, and in the summer she died at home.

On adm., April 27, 1928: Weight 22.700 kg.

On disch., May 11, 1928: » 21.800 »
÷ 900 gm.

Height Febr. 23, 1928: 118.5 cm.

» April 28, 1928: 118.5 «

Case Records of Chronic Dyspepsia.

No. 1. — Girl. Reg. No. 165/1930. Born Nov. 22, 1929.

2 months.

Adm. Jan. 2, 1930.

Disch. April 6, 1930. Blood sugar exam. Jan. 24, 1930.

Clinical diagnosis: Gastro-enteritis. Achylia gastrica.

Bottle baby. Has not been thriving well. During the week prior to the adm., poor appetite, thin stools, greenish in colour; also a moderate degree of cold.

On adm.: Little child, thin and poor. Turgor markedly lowered; complexion pale; fontanels slightly depressed; no signs of rickets.

Under the treatment the patient improved considerably. Test meals (barley water), on Jan. 11 and 20, showed achylia, whereas normal values were obtained on Febr. 18. For a couple of months there was still a tendency to voluminous and loose or pasty stools. Urine: No abnormalities.

Weight on adm., Jan. 2, 1930 3.260 kg.

» » disch. April 6, 1930 4.880 »
+ 1.620 «

No. 2. — Girl. Reg. No. 496/1929. Born Nov. 22, 1928.

5½ months.

Adm. April 23, 1929.

Disch. May 21, 1929. Blood sugar exam. May 8 and 16.

Clinical diagnosis: Dyspepsia chronica. Rachitis.

Breast-feeding the first month, then increasing milk-mixtures 2—3 months before the admission, loss of appetite and weakness, together with a moderate cold. The patient is said to have been treated for anæmia with iron.

On adm.: Flabby and thin child, with lowered turgor, slight degree of rachitic rosary and epiphyseal swelling, but no other signs of rickets. The child is pale, and has difficulty in keeping warm. Her appetite is very poor. Fæces white and pasty. No fever. Test meal (barley water): Normal findings. Urine: No abnormalities.

She improved considerably on a diet of 3 parts milk + 1 part barley water + 0.6 % lactic acid, together with irradiated ergosterin (Vigantol), 10 drops daily.

Weight on adm., April 25, 1929: 6.350 kg.

» » disch., May 21, 1929: 6.550 »
+ 200 gm.

No. 3. — Boy. Reg. No. 293/1930. Born Nov. 20, 1929.

6 months.

Adm. Febr. 5, 1930.

Disch. June 3, 1930. Blood sugar exam. May 12 and 17.

Clinical diagnosis: Dyspepsia chronica.

Breast-fed the first month. One month before adm., the patient was getting ill, with vomiting during and after the meals, and tendency to constipation.

On adm.: The child is thin, pale, with lowered turgor. No signs of rickets. The abdomen is normal, apart from a slight degree of umbilical hernia. To begin with, the child kept on regurgitating the food; but this tendency subsided considerably during his stay in the hospital. The stools were first loose and lumpy, but gradually they became white and pasty. The patient was treated with lactic acid. Test meals (barley water) on February 8 and May 5 showed normal values. Urine: No abnormalities.

Weight on adm. Febr. 5, 1930: 4.080 kg.

» » disch. June 3, 1930: 6.200 »
+ 2.120 »

No. 4. — Girl. Reg. No. 414/1930. Born Oct. 5, 1929.

$\frac{1}{2}$ year.

Adm. April 24, 1930. Blood sugar exam. May 15 and 22.

Disch. Aug. 24, 1930.

Clinical diagnosis: Dyspepsia chronica. Rachitis.

Breast-fed first 3 months. The illness began 3 months before the admission, subsequent to an attack of chicken-pox. Since then, she has been thriving poorly, regurgitating her meals. The bowels have been regular. She catches cold very readily.

On adm.: The child is small and thin, with poor turgor, flabby muscles, and signs of rickets. Mental development normal for her age. The stools are at first rather scarce and pasty, later very large, whitish-grey and greasy.

2 months after adm.: No particular change in the condition. The abdomen is large. In spite of treatment with irradiated ergosterin (Ultranol) and cod liver oil, there is still a marked degree of rickets. Light therapy prescribed.

On disch., 4 months after adm.: Good results from the light therapy, the rickets being finally cured. The child has improved very much. The stools have been normal the past month. She is now on a diet of milk mixtures and gruel. Test meal (May 14): Normal findings.

Weight on adm., April 24, 1930: 5.250 kg.
» » disch., Aug. 24, 1930: 6.500 »
+ 1.250 »

No. 5. — Boy. Reg. No. 373/1930. Born Jan. 7 1929.

14 months.

Adm. March 3, 1930. Blood sugar exam. July 14 and 17.

Disch. July 23, 1930.

Clinical diagnosis: Colitis chronica. Rachitis.

Bottle-baby. The child was taken ill one week before adm. with cough and shortness of breath. Admitted for bronchopneumonia. He had been thriving poorly, but nothing particular had been noticed as to the stools.

On adm.: The child is small and thin, with poor turgor, pale colour of face and mucous membranes, rather marked rickets. Pneumonia on both sides.

The pneumonia cleared up in about one week. At first the stools were very slimy, lumpy and light in colour. Under dietary treatment the stools were normal for a while; but as soon as this treatment was discontinued, they again became loose and slimy, thin and stinking. During his stay in the hosp., the patient had several colds with coughing and coryza.

3 months after adm.: Stools large and greasy.

On disch.: Appetite fair. No cold. Hæmoglobin 80 %. Only inconspicuous signs of rickets. Abdomen rather large. Otherwise no abnormalities. Bowels regular, stools normal. Test meal (June 20): Normal findings.

Weight on adm., March 3, 1930: 9.000 kg.

» » disch., July 23, 1930: 9.300 »
+ 300 gm.

CRETINISM.

Introduction.

Myxoedema in adults is generally stated to be associated with an increase of the glucose tolerance, so that the elementary hyperglycæmia after glucose ingestion is less pronounced in these patients than in normal individuals (Strauss¹¹³), von Noorden & Isaac⁸⁸, Janney & Isaacson⁵⁷). After thyroid treatment, however, the last authors found normal values. On the other hand, Gardiner-Hill, Brett & Forest-Smith³⁴ have studied the blood sugar regulation in 15 myxoedematous adults (34—60 years old) by ingestion of 50 gm. glucose in 100 cc. water, and they found the hyperglycæmia to be greater and more protracted in these patients than in normal individuals. Thus they found an average maximal value of 0.214 % in one hour after the glucose ingestion. As there was no glucosuria, they assumed that the threshold value in these cases was increased. As other investigators, they found the fasting blood sugar values in myxoedematous patients to fall within the normal limits. They further found that the administration of thyroid gland makes the blood sugar curve lower and shorter.

Hyperthyroidism, on the other hand, is very often associated with glycosuria and hyperglycæmia (Krabbe⁶⁴, Strauss¹¹³, von Noorden & Isaac⁸⁸, Janney & Isaacson⁵⁷, Joslin⁶⁰).

Torday¹²¹ examined the glucose tolerance in 4 cases of hyperthyroidism in adults by ingestion of 30 gm. glucose (blood taken 20 — 40 — 80 — 120 — 180 minutes after glucose ingestion; Hagedorn-Jensen method) and found the hyperglycæmia to be increased and protracted; in one of these

cases the maximal value was 0.225 %, and the hyperglycæmia lasted more than 3 hours. Gardiner-Hill, Brett & Forest-Smith³⁴ have likewise found an increase in the height and duration of the blood sugar curve in severe cases of hyperthyroidism, frequently associated with glycosuria.

Therapeutic administration of thyroid gland extract has sometimes been followed by glycosuria (von Noorden & Isaac⁸⁸, Strauss¹¹³). In experiments on rabbits, Abelin & Goldner¹ found no rise of the blood sugar concentration after ingestion of levulose; but when thyroid gland had been given for some time, ingestion of levulose produced a marked hyperglycæmia.

I have not been able in the literature to find any studies on the blood sugar regulation in cretins.

Own investigations.

The blood sugar regulation after glucose ingestion was examined in 4 cretins, aged 1—4 years. 2 of these children, 1 and 2 years old, had 2 gm. glucose per kg. of body weight. The other two had 1.5 gm. glucose per kg. In all 4 cases there had been no treatment with thyroid gland prior to the first blood sugar examination, or treatment of this kind had not been given for several months prior to the examination.

The fasting values (before thyroid treatment) varied between 0.067 and 0.085 %, giving an average of 0.074 % — that is, rather low fasting values.

Before treatment with thyroidin, the glucose ingestion was followed by a rather small rise of the blood sugar concentration, yet within the normal limits. The maximal values varied from 0.110 to 0.154 %, with an average of 0.133 %. The hyperglycæmic period was not particularly protracted except in one instance (first examination in case No. 2) where the fasting value was hardly reached in 2½ hours after the glucose ingestion. There was no tendency to hypoglycæmia after the blood sugar curve returned to the fasting level. Apart from

this, the blood sugar curves after glucose ingestion were very irregular in No. 2 and No. 4, whereas their appearance did not show any peculiarities in the other two cases.

After treatment with *thyroidin*, the blood sugar regulation was examined in cases No. 1 and 2 — in No. 1 after one month's treatment, in No. 2 after 11 days' treatment. It turned out that the blood sugar rise after the same amount of glucose was very much greater now than before the treatment. In No. 1, the maximal value obtained in one of these tests was 0.254 %, and here the blood sugar concentration stayed above 0.200 % for ca. 70 minutes. In the next test, the maximal value

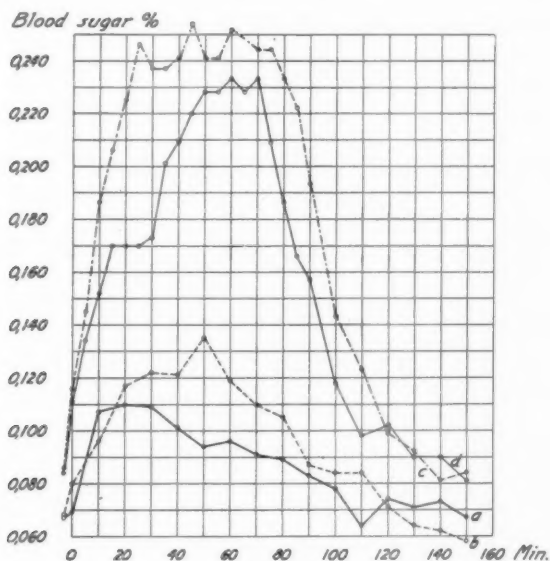


Fig. 68.

Cretinism, No. 1. Female.

Age: 1 year

Before thyroid treatment:

a, March 25, 1930. 2 gm. gluc. per kg.

b, " 28, " 2 " " " "

After thyroid treatment:

c, April 26, 1930. 2 gm. gluc. per kg.

d, May 10, " 2 " " " "

was 0.233 %, and the blood sugar concentration stayed above 0.200 % for 40 minutes (Fig. 68). There was no subsequent hypoglycaemia in either of these tests. In No. 2, the maximal values obtained were respectively 0.244 and 0.204 %. In this case, too, there was no subsequent hypoglycaemia (Fig. 69). Expressed in the term of blood sugar rise, the tests before thyroidin treatment showed in No. 1 a rise of 0.033 and 0.067 % respectively, and after thyroidin treatment, a rise of 0.170 and 0.147 %; in No. 2 the blood sugar rise before thyroidin treatment was 0.082 and 0.050 %, while after thyroidin treatment it was 0.149 and 0.133 % respectively.

In No. 1, the first test after thyroidin treatment was accompanied by glycosuria.

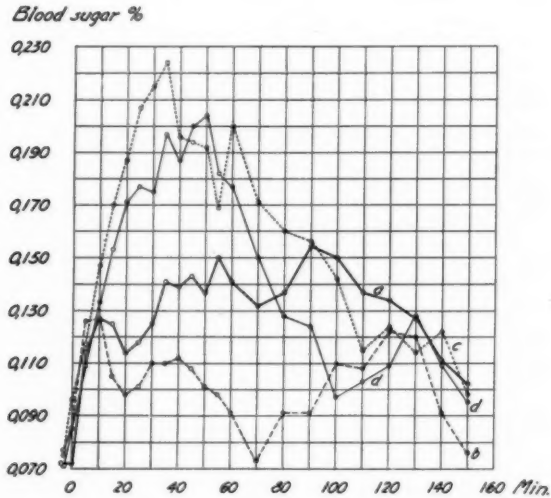


Fig. 69.

Cretinism, No. 2. Male.
Age: 2 years.

Before thyroid treatment:

a, July 4, 1930. 2 gm. gluc. per kg.

b, " 7, " 2 " " " "

After thyroid treatment:

c, July 19, 1930. 2 gm. gluc. per kg.

d, " 23, " 2 " " " "

In No. 1, a test, prior to the thyroidin treatment, with 0.3 cc. 1 ‰ adrenalin (subcutaneously) showed a gradual rise of the blood sugar concentration to 0.134 % within 50 minutes, and then an equally gradual fall in the next 1½ hour with an end value of 0.058 % — that is, a »normal« curve.

As to the thyroidin effect on the fasting blood sugar values, they were in No. 1 before the treatment 0.067 and 0.068 %, after the treatment 0.084 and 0.086 %. In No. 2, the fasting blood sugar values were all the time at the same level (from 0.071 to 0.077 %) before as well as after the treatment, so these 2 cases show no definite effect of the treatment upon the fasting blood sugar concentration.

In No. 3, unfortunately, the tests had to be discontinued

Table 18.
*Glucose Tolerance Tests in Cretinism before and after
Thyroid Treatment.*

(4 children, aged 1—4 years; 11 tests with 2 gm. gluc. per kg.).

	Average ‰	Variations ‰
Fasting values, before treatment....	0.074	0.067—0.085
» » after »	0.079	0.071—0.086
Maximal values before »	0.133	0.110—0.154
» » after »	0.229	0.204—0.254
Rise of blood sugar before » No. 1		0.043—0.067
» » after » »		0.147—0.170
» » before » No. 2		0.050—0.082
» » after » »		0.133 - 0.149
Time of max. val. before » (min.)		10—90
» » after » »		35—60
Duration of hyperglycæmia before treatm.	110	50—150
» » after treatm.	125	100—150

because the patient got whooping-cough. As to No. 4, at the time he was examined I had not yet thought of investigating the blood sugar regulation after the institution of thyroid treatment.

These findings show that *in cretinism the ingestion of glucose gives but a rather low rise of the blood sugar curve (corresponding with the findings of other investigators in myxoedema in adults)*. After treatment with thyroidin for some time, however, ingestion of the same dose of glucose gives an extremely marked degree of hyperglycæmia.

Thus, treatment with thyroidin has a very marked influence upon the blood sugar regulation in cretinism. This effect is highly suggestive of the increased alimentary hyperglycæmia so frequently demonstrated in patients with hyperthyroidism.

Case Records of Cretinism.

No. 4. — Girl. Reg. No. 248/1930. Born March 25, 1929.

1 year.

Adm. March 20, 1930. Blood sugar exam. March 25 and 28, April
26, May 10, 1930.

Disch. May 18, 1930.

Two female relatives on the father's side are said to have suffered from hyperthyroidism; one brother, a year older, is a cretin.

Present illness: ca. 3 months before her admission to the hospital, her parents realized that the child did not develop normally. Her voice was gradually becoming very coarse; the tongue was large; and gradually the abdomen was also enlarging. The child was able to recognize her surroundings, play and sit upright, but she was unable to stand on her feet, not even with support.

On adm.: The child is little, measuring only 64 cm. — the height of a normal child at the age of 6—7 months — and weighing 8.000 kg. The extremities are short and thick; the voice is coarse and hoarse; the hair is thin, dry and brittle. The back of the head is bald; the face puffy, especially around the eyes; the tongue is large and thick. There are no teeth. The neck is short and thick. The thyroid gland is not palpable. The abdomen is large, with protruding umbilicus; no palpable enlargement of organs; no other intumescence.

The child had a good appetite; the bowels were regular. She was capable of fixation and smiling.

X-ray exam., March 22: Findings similar to those in a new-born child, there being no signs whatever of the centres of ossification. Slight rachitic changes in the bones.

March 29.

Rx Tabl. Gl. thyreoid.

50 units daily.

After the child had been treated about a month with thyroïdin, she had improved considerably. She was more lively, and she was now able to stand on her feet when supported. Her voice was nearly

natural. She was smiling, and she watched her surroundings with interest. After a primary loss in weight, at the institution of thyroid treatment, she was now gaining in weight. The skin was warm and slightly perspiring. Hæmoglobin 80 % (on adm. 74 %). The appearance of the patient was yet considerably myxoedematous, but, on the whole, far less than on adm. The improvement was more pronounced yet, when the child was discharged after 1½ month of thyroid treatment.

On adm., March 20, 1930: Weight 8.000 kg. Height 64 cm.

On disch., May 18, 1930: » 8.650 » » 64 »
 + 650 gm.

No. 2. — Boy. Reg. No. 375/1930. Born July 21, 1928.

2 years.

Adm. June 24, 1930. Blood sugar exam. July 4, 7, 19 and 23.

Disch. July 23, 1930.

Family history negative. The patient is the youngest of 3 children.

Present illness: The first evidence of the lesion was noticed a few weeks after birth, when the child was strikingly dull and inactive. When the child was 8 or 9 months old, his condition was diagnosed as cretinism by the family physician, and he was treated with thyroidin. At the age of 11 months, he was admitted to this department, June 22, 1929, where he stayed till July 3. *X-ray exam.* showed marked retardation in the development of the centres of ossification of the carpal bones, the findings corresponding to those in a normal child of 4—5 months. He was discharged with tabl. gl. thyreoid., 100 units \times 2 daily, and he was under this treatment at home for about a year. During this period, he was progressing but slowly; he was able to stand on his feet when supported and crawl around, but he was unable to walk. He was habitually constipated, treated with liquid paraffin. Mentally he kept on being backward.

On 2. adm., June 24, 1930: The patient is now about 2 years old. His appearance is markedly cretinic. He has a broad and flat nose, and a large tongue that is nearly always protruding from the mouth. The skin is dry, with light yellow pigmentations, especially on the hands. The growth of hair is good, the hair being soft, glossy and curly, fairly thick. The extremities are short and thick; the nails are normal. The thyroid gland is not palpable. The voice is coarse and hoarse. The anterior fontanel measures 3×3 cm. No signs of

rickets. The teeth, 4/3, are small and deformed, with thin and defective enamel. The abdomen is rather large, with protruding umbilicus, but no real hernia.

X-ray exam. of the carpal bones shows still a marked retardation in the development of the centres of ossification, the findings corresponding to those in the normal child of ca. 5 months.

The child does not give the impression of being imbecile, as he watches his surroundings with interest and plays of his own accord. He babbles a lot, but can not say articulated words. He is able to sit upright, and he can stand on his feet and walk when supported; but he is altogether uncleanly.

July 8.

Rx Tabl. Gl. thyreoid.

200 units \times 2 daily.

When discharged, after 2 weeks of thyroid treatment, he was much more active and bright, playing a great deal and standing well on his feet; and he looked much less like a cretin. *X-ray exam.* showed now a normal development of the carpal centres of ossification.

On adm., June 24, 1930: Weight 12.400 kg. Height 78 cm.

On disch., July 23, 1930: » 12.200 » » 80 »
 \div 200 gm. + 2 cm.

No. 3. — Girl. Reg. No. 610/1930. Born Febr. 14, 1928.

2 $\frac{3}{4}$ years.

Adm. Nov. 4, 1930. Blood sugar exam. Nov. 14, 1930.

Disch. Dec. 17, 1930.

Family history negative. The patient is the youngest of 7 children. She was born at full term, by natural delivery, and was breast-fed for $\frac{1}{2}$ year.

Present illness: From early infancy she has been lagging in development. Since one year old, she has been suffering from constipation. One year before the admission, her parents consulted a physician, who has since been treating the child with »tablets«, which the parents think have been of some use.

On adm., the child, nearly 3 years old, has the height of a normal child of 1 $\frac{1}{2}$ year and the weight of a one-year-old (height 75 cm., weight 10.900 kg.). Her appearance is cretinic. She has a large tongue, dry skin (wrinkled on the hands and lower extremities) but normal hair. The anterior fontanel measures 3 \times 4 cm. The abdo-

men is flabby and rather large, with protruding umbilical hernia and diastasis of the recti abdominis.

X-ray exam. (on adm.): Marked retardation in the development of the carpal centres of ossification, corresponding to the age of 2–3 months.

Mentally, at times she is very apathetic, at other times she shrieks continuously; yet the look in her eyes is alert and sensible. Her voice is coarse. Her appetite is poor.

Thyroid treatment was instituted (Tabl. gl. thyreoid., 100 units daily). But soon after her admission, she had a severe cold, accompanied by fever, and it turned out to be whooping-cough. In spite of her infection and febrile condition during most of the thyroid treatment, she improved very much as to appearance and general condition. She was transferred to the hospital for contagious diseases.

On adm., Nov. 4 1930: Weight 10.900 kg. Height 75 cm.

On disch., Dec. 17, 1930: » 11.100 » » ?

+ 200 gm.

No. 4. — Boy. Reg. No. 90/1930. Born Sept. 28, 1925.

$4\frac{1}{4}$ years.

Adm. Jan. 8, 1930. Blood sugar exam. Jan. 22 and 27.

Disch. Febr. 22, 1930.

One great-grand-mother died of hyperthyroidism. One aunt is operated for hyperthyroidism. One younger sister is a cretin.

Present illness: The patient has always been lagging a great deal, mentally as well as physically, but has never had any other illness. He was not able to walk until he was 2 years old. He has not been treated with thyroid, as the diagnosis of his illness has not been made before.

On adm.: Height $82\frac{1}{2}$ cm., weight 12.700 kg. — that is, corresponding with the findings in a normal child of 2 years. His appearance is typically cretinic, though to a moderate degree. There are signs of previous rickets. The abdomen is large, with protruding umbilical hernia. The extremities are rather short. The face is puffy, with a little flat nose and large lips. The milk teeth are present in normal number, but they are small and far apart. The skin is dry; the hair is thin; the nails normal; and the testes unusually large. The voice is coarse and hoarse. Mentally, the child is very dull, but not imbecile; yet he can not talk.

X-ray exam.: Centres of ossification of carpal bones corresponding to the findings in a one-year-old child. No signs of rickets in the distal epiphyses of the forearm.

After one month of thyroid treatment (100 units \times 2 daily) he improved very markedly, taking interest in the surroundings and learning to say a few words; his appearance was less cretinic, too.

On adm. Jan. 8, 1930: Weight 12.700 kg. Height $82\frac{1}{2}$ cm.

On disch.,	Febr. 22, 1930:	»	14.000	»	»	$84\frac{1}{2}$	»
			+ 1.300	»		+ 2	»

ECZEMA.

(Exudative Diathesis).

Previous investigations.

In 1928, Herlitz⁵⁰ published a comprehensive investigation on the blood sugar regulation in infants, with special reference to the conditions in exudative diathesis. Prior to this work, there were but scattered data on abnormalities of the blood sugar regulation in infants suffering from skin lesions, especially eczema (Mertz & Rominger⁵⁰ and Lindberg⁷¹).

Herlitz' material comprises 21 infants, aged from 3 weeks to 11 months, suffering from exudative diathesis with skin eruption. He used the Hagedorn-Jensen method, and for standard dose he gave 1.5 gm. glucose in 10 % watery solution per kg. of body weight, after 5 hours' fasting. In the first hour after the glucose ingestion, samples of the blood were taken every 15 minutes, in the next 3 hours every 30 minutes, so that the examination period is 4 hours. None of the children had shown any symptoms of dyspepsia; especially, the bowels were regular, so there is no reason to think that in some of these cases the mucous membrane of the intestines might have been irritated or swollen. By this, Herlitz had in view especially a hypothesis advanced by Mertz & Rominger⁵⁰; that exudative diathesis is associated with a swelling of the mucous membrane of the intestines, giving an increase in the permeability to sugar, which in turn produces the higher blood sugar curves.

In children with exudative diathesis, examined in this way, Herlitz found the maximal blood sugar value varying between

0.115 and 0.224 %, with an average of 0.16 %. For comparison he gives a normal material, in which the highest maximal value is 0.162 %, and the average maximal value 0.123 %. In 5 cases the maximal value was higher than he had ever observed in normal children. In these 5 cases, the patients were children in whom the skin eruption had been present only 2 weeks or less.

To rule out the influence from the gastro-intestinal tract, Herlitz made the examination in some cases after subcutaneous administration of the glucose, giving 0.3 gm. glucose per kg. in 10 % watery solution after a fasting period of 5 hours. 17 children were examined in this way. In cases where the skin eruption had persisted for 2 weeks or more, the blood sugar curve was practically the same as found in normal children (control material, 10 normal infants). But, in cases where the eruption had been present only 1 week or less, he found that the rise of the blood sugar concentration was higher — up to 0.150 % — and that the blood sugar value did not return to the initial value in $2\frac{1}{2}$ hours after the glucose administration. In a couple of cases, where the blood sugar curve was examined one week after the onset of the skin eruption, and 4 weeks later, when most of it had disappeared, Herlitz found the last blood sugar curve to be much lower than the first, after oral ingestion as well as after subcutaneous administration.

From his findings, Herlitz concludes that in children with exudative diathesis, when the skin eruption has persisted for more than 2 weeks, the blood sugar curve after glucose ingestion runs practically the same course as in normal infants; but, when the skin eruption is not 2 weeks old, the blood sugar values come higher, with an average maximal value of ca. 0.16 %, although the duration of the hyperglycæmia is not increased, as usually the blood sugar curve returns to the fasting level in 2—3 hours.

The tables of Herlitz show, however, that in 2 cases where the skin eruption has lasted but 1 week, the glucose ingestion gives maximal values of only 0.155 % and 0.133 %. According-

ly it is no absolute rule that the blood sugar values are very high during the first part of the skin eruption.

Herlitz attributes the abnormal blood sugar finding in children with exudative diathesis to an increase in the tonus of the vegetative nervous system, especially the liver region. He thinks that the accentuation of tonus is due to the skin eruption, whereas he thinks the reverse is rather improbable.

Own Investigations.

The material comprises 5 children with exudative diathesis, eczema persisting from 5 days to 9 months. The age of these children was from 3 to 15 months. The technique of examination was the same as usual, the children taking 2 gm. of glucose per kg. of body weight in 10 % watery solution after fasting 6—6½ hours. Table 19 gives an abstract of the results obtained.

The highest fasting value, 0.101 %, was found in a child (No. 4), in whom the skin eruption had been present but 4 days. 4 days later, the same child showed a fasting value of 0.096 %. In the other cases — where the skin eruption had been present at least one month — the fasting values were all less than 0.090 %, agreeing with the fasting values in normal children of the same age.

The child, in whom the skin eruption was less than 2 weeks old, showed on the first examination a maximal blood sugar value of 0.226 %, and on the next examination, 4 days later, a maximal value of 0.164 % — respectively, 40 and 20 minutes after the glucose ingestion. This child was examined again when the skin eruption had persisted for 1 month; and this time the maximal value was 0.240 %. In this case the maximal value was accordingly highest when the skin eruption had persisted for more than 2 weeks. In another child where the skin eruption had persisted for about 1 month, 2 blood sugar tests at an interval of 1 week gave the respective maximal values of 0.206 and 0.201 %; and in one case where the eruption

had persisted for 2 months, the maximal value was 0.183 %. A child, 6 months old, showing the first eruption of eczema at the age of $4\frac{1}{2}$ months, gave maximal values of 0.216 and 0.196 % on blood sugar examination 3 days apart. Finally, in one case where the eczema had persisted for 9 months, the maximal values were 0.120 and 0.139 %.

In No. 3 — aged 6 months, with eczema of $4\frac{1}{2}$ months' duration — the blood sugar curve stayed on values above 0.200 % for 35 minutes. Apart from this, the configuration of

Table 19.
Glucose Tolerance Tests in children with Eczema.

Pt. No.* Age. Date of Exam.	Dura- tion of Eczema.	Test Dose**	Fast- ing Value ‰	Maxi- mal Value ‰	Rise of Blood Sugar ‰	Time of Max. Val. min.	Duration of Hy- perglyc- æmia. min.
No. 4. 6 m.							
3-4-30	4 days	2 gm. gluc.	0.101	0.226	0.125	40	110
3-8-30	8 »	2 » »	0.096	0.164	0.068	20	140
4-1-30	1 mth.	2 » »	0.089	0.240	0.151	40	120
No. 1. 3 m.							
9-5-29	1 mth.	2 gm. gluc.	0.084	0.206	0.122	50	110
9-12-29	5 weeks	2 » »	0.075	0.201	0.126	35	100
No. 2. 5 m.							
2-21-29	2 mths.	2 gm. gluc.	0.080	0.183	0.103	35	76
No. 3. 6 m.							
2-19-29	$4\frac{1}{2}$ mths.	2 gm. gluc.	0.086	0.216	0.130	60	135
2-22-29	» »	2 » »	0.073	0.196	0.123	50	80
No. 5. 15 m.							
2-5-30	9 mths.	2 gm. gluc.	0.087	0.120	0.033	15	20
2-21-30	9 »	2 » »	0.081	0.139	0.058	25	50

*) The consecutive order of the patients in the table is determined by the duration of the eczema, not as usual by the age of the patient. The Nos of the patients refer to their age and consecutive order in the case records.

**) Grams per kilogram of body weight, given by mouth.

the blood sugar curve in these patients did not differ in any particular respect from that observed in normal children.

So it is evident from these tests that *a maximal value above 0.200 % after ingestion of 2 gm. of glucose per kg. of body weight may be present somewhat more frequently than in normal individuals (here, in 5 out of 10 individuals); but apart from this, the rise of the blood sugar curve does not exceed the maximal values frequently found subsequent to the same dose of glucose in normal children.* The high maximal values do not appear to be dependent upon any fixed period of the eruption (less than 2 weeks, as emphasized by Herlitz⁵⁰).

Case Records of Eczema (Exudative Diathesis).

No. 1. — Boy. Reg. No. 462/1929. Born May 17, 1929.

3 months.

Adm. Aug. 26, 1929. Blood sugar exam. Sep. 5 and 12.

Disch. Oct. 20, 1929.

Clinical diagnosis: Eczema. Urticaria. Anæmia.

The child was born ca. 1½ month before term. He had breast milk the first 2½ months, later milk mixtures. 1 month before adm.: pin-head-sized red points, appearing first on the buttocks, later in the face and the scalp, and then on the extremities. No tendency to colds.

On adm.: The child is fairly well-developed; nutrition fair. No signs of rickets. Everywhere on the skin except on the cheeks and the palms, is a skin lesion consisting in small spots or in larger confluent areas, scaly and, in all the folds, exudative. The tongue looks normal. Glandular swelling on both sides of the neck.

Under treatment with salve (anthrarobin, zinc oxide) the skin lesion is cured in about 1½ month. Now and then, small eruptions appear on the face or on the trunk, resembling measles, sometimes with small vesicles. These eruptions last as a rule only about 1 hour. No fever.

On disch.: Normal appearance; no signs of rickets; the skin looks perfectly normal throughout.

Weight on adm. Aug. 26, 1929: 4.100 kg.

» » disch. Oct. 20, 1929: 5.250 »

+ 1.150 »

No. 2. — Boy. Reg. No. 146/1929. Born Sept. 11, 1928.

6 months.

Adm. Febr. 19, 1929. Blood sugar exam. Febr. 21.

Disch. March 31, 1929.

Clinical diagnosis: Eczema.

The child was breast-fed the first 4 months, then kept on milk mixtures. 2 months before adm.: Onset of a reddish, knobby and scaly exanthema, moist in some areas, scattered over the face and the scalp. No particular tendency to colds.

On adm.: Height and weight corresponding to the normal for his age; turgor good. On both cheeks, the skin is red, inflamed, exudative, with several small vesicles. A similar affection is seen on the forehead and in the scalp. On the legs the skin is dry, rough and scaly. The tongue is normal. Enlargement of cervical glands. No signs of rickets. Treated with wet compresses and zinc oxide salve; the skin lesion is cured, but there is persistently a tendency to scalliness and itching papules. Otherwise the child is perfectly healthy. Diet consisted in milk mixtures.

Weight on adm. Febr. 19, 1929: 7.780 kg.

» » disch. March 31, 1929: 7.950 »

+ 170 gm.

No. 3. — Boy. Reg. No. 142/1929. Born Aug. 5, 1928.

6 months.

Adm. Febr. 4, 1929. Blood sugar exam. Febr. 19 and 22.

Disch. March 30, 1929.

Clinical diagnosis: Eczema.

The child was breast-fed the first 2 months, then kept on milk mixtures and gruel. Even when he had mother's milk, the entire scalp was the site of numerous pinhead-sized papules, some moist, some scaly. No particular susceptibility to colds.

On adm.: Large, vigorous child, in good nutritional condition; but turgor rather lowered. No signs of rickets. Throughout the scalp and in the greater part of the face the skin is studded with the mentioned papules. Moderate enlargement of the cervical glands. The tongue looks normal.

Under treatment with wet compresses and, subsequently, with zinc oxide salve, the skin lesion improved rapidly; but 2 weeks after the admission, there was a relapse. Under the same treatment as before, the skin lesion improved again, with relapses now and then during his stay in the hospital. There was no fever in the hospital. Diet: Milk mixtures and gruels.

Weight on adm. Febr. 4, 1929: 7.700 kg.

» » disch. March 30, 1929: 8.100 »

+ 400 gm.

No. 4. — Boy. Reg. No. 191/1930. Born Aug. 31, 1929.

6 months.

Adm. March 3, 1930. Blood sugar exam. March 4 and 8, and April 1.

Disch. April 18, 1930.

Clinical diagnosis: Prurigo infantilis. Eczema.

The first 6 weeks of life, the child had mother's milk, then milk mixtures. 3—4 days before adm.: Itching, skin eruptions on the forehead and cheeks. No history of susceptibility to colds.

On adm.: The child is large for its age, rather fat, without any signs of rickets. He has no teeth. The tongue looks normal. The entire face and scalp is the site of a reddish exanthema, in some places scaly, in other places moist, with markings of scratchings. On the trunk and extremities, the skin is normal.

The skin lesion was subject to very great variations, sometimes disappearing almost completely, at other times recurring with reddish, granular, intensely itching points, usually moistening. Treated with wet compresses.

On disch.: The skin looks healthy, except on the forehead, where there is still some slight tendency to scaliness.

No fever. Diet: milk mixtures and gruels.

Weight on adm. March 2, 1930: 8.590 kg.

» » disch. April 18, 1930: 8.450 »

÷ 140 gm.

No. 5. — Boy. Reg. No. 104/1930. Born November 4, 1928.

1¼ year.

Adm. Febr. 11, 1930. Blood sugar exam. Febr. 15 and 21.

Disch. Febr. 28, 1930.

Clinical diagnosis: Prurigo infantilis (Besnier).

Breast-feeding first 6 months, then milk mixtures, and last 4 months gruel, mashed potatoes, oatmeal gruel. At the age of 6 months, an itching skin eruption on the dorsal surface of both knees; later similar affection in both elbows and poples, beginning as small red spots which are confluent rapidly, so that each location is soon the site of a diffuse redness. He had been treated for some time at home with discontinuation of milk and animal proteins, getting in addition a calcium preparation, but without any effect. He has not been susceptible to colds.

On adm.: Nutrition fair; development corresponding to the age. No signs of rickets. Teeth 6/6. Tongue looks normal. The skin of the body looks normal. But on both cheeks, before and back of the ears,

is a moist papular exanthema, with some hæmorrhages from recent scratchings. In the scalp are areas of similar, scaly, reddish skin eruptions. Similar skin lesions are observed on the back of both hands, in the cubits and poples and inguens. The turgor of the skin is good. Tongue slightly coated. Moderate degree of cervical adenitis. No rise of temperature. Treatment with zinc oxide paste and tar ointment. Under this treatment, the skin lesion subsided, but there is still some itching.

Weight on adm. Febr. 11, 1930: 10.350 kg.

» » disch. Febr. 28, 1930: 11.150 »

+ 800 gm.

RICKETS — TETANY.

Previous Investigations.

König & Lenart⁶⁷ have stated that in rachitic children the blood sugar curve is higher and of greater duration than in normal children; on the other hand, the sugar tolerance, according to these authors, is increased in tetany, so that in this condition the blood sugar curve is lower, and the hyperglycæmia of shorter duration. These authors examined the blood sugar in 8 rachitic children after ingestion of 2.5 gm. glucose per kg. of body weight in 10 % solution (Bang method; samples taken every 20—30 minutes through 2 hours). The authors state that in rachitic children the fasting blood sugar values were within normal limits (ranging from 0.070 to 0.103, averaging 0.083). After glucose ingestion they find the maximal values ranging from 0.134 to 0.187 %, averaging 0.162 %, with an average duration of the hyperglycæmia of 90 minutes. In their control material, after the same glucose ingestion, they find an average maximal value of 0.114 %, and the highest maximal value is 0.148 %; the curves return to the fasting level in 50 minutes. But their control material comprises only 4 infants. One rachitic child was suffering from tetany, showing in addition a blood sugar curve on a lower level than the other cases. From their findings, these authors conclude: »Die Prüfung der alimentären glykämischen Reaktion deckte bei Rachitis, bei normal gebliebener endogener Zuckerregulation, eine Störung der exogenen Zuckerregulation auf. Die Ursache dieser Störung ist entweder in dem gesteigerten Tonus des

sympathischen Nervensystems bzw. in der dies begünstigenden Verschiebung des hormonalen Gleichgewichtes, oder aber in der herabgesetzten Zuckeraufnahmefähigkeit der Gewebe zu suchen.« Their values however fall within the normal limits, so they do not allow of any conclusive inferences.

Landsberger & Silber⁶⁸ examined the blood sugar curve in 6 children after subcutaneous administration of glucose (Hagedorn-Jensen method of glucose determination), and these authors too find a greater increase in the blood sugar rise during rickets than during tetany.

Own Investigations.

A. Rickets.

The material covers 5 children with uncomplicated, fully developed, rickets, at the age of 6—8 months when their blood sugar regulation was examined. In each case the dose of glucose was 2 gm. per kg. in 10 % watery solution. 3 of the children were examined two times. In these children, the fasting values varied from 0.057 to 0.102, with an average of 0.078 %. 0.057 % is a rather low fasting value. On 2 examinations this child showed fasting values respectively of 0.057 and 0.059 %. In the other children, the fasting values did not differ from

Table 20.
Blood Sugar Curve in Children with Rickets.
(5 children, aged 6—8 months; 8 examinations).

	<i>Average</i>	<i>Variations</i>
Fasting Value %	0.078	0.057—0.102
Maximal values %	0.172	0.140—0.201
Rise of Blood Sugar %	0.094	0.054—0.109
Time of maximal value		
after glucose ingest. in min. 33		20—55
Duration of hyperglycæmia		
in min. 103		80—120

what is found in normal children. *After glucose ingestion, the maximal values, the duration of hyperglycæmia, and fall to hypoglycæmic values do not differ from the findings in normal children of the same age.*

B. Tetany.

Blood sugar examination is made on 6 children with tetany, aged from 6 to 16 months. In each case the tetany was complicated with rickets (see case records, p. 169). The first blood sugar examination was made during marked symptoms of tetany; no more examinations are made in No. 2 and 4. In No. 1, 3, 5 and 6 blood sugar examination is made too after all symptoms of tetany had subsided.

As to the fasting values, 1 case (No. 1) showed on the first examination the peculiarity of a fasting value of 0.045 %. The examination was repeated on the next day, showing a fasting value of 0.063 %. Subsequent examinations, as the patient was improving, gave fasting blood sugar values of 0.090 % — and one week later 0.069 %. The fasting blood sugar values were low too in the other cases of tetany, though not so markedly as in this case. Thus, in 5 out of 9 determinations, the fasting values are less than 0.070. The average value of the 9 determinations were 0.069 %, with variations from 0.045 to 0.077 %. As far as I know, this tendency to low fasting values of the blood sugar in children suffering from tetany has not been reported before. In children suffering from spasms not due to tetany, Griffith ⁴⁰ has in some cases found fasting blood sugar values as low as 0.020 and 0.057 %, during attacks of spasm as well as without.

As these children recovered, the fasting blood sugar values varied from 0.069 to 0.090 %, with an average of 0.076 %.

The blood sugar curve after glucose ingestion shows no peculiarities worth mentioning. In one case, No. 1, the maximal values are highest on the first 2 examinations, made when symptoms of tetany were present; the next 2 examinations,

after the patient has recovered, show lower maximal values. The reverse however is observed in case No. 3.

In these cases there does not appear to be any marked tendency to hypoglycæmia after the alimentary hyperglycæmia produced by glucose ingestion. Still, on the second blood sugar examination, in case No. 1, during a period of manifest tetany, the blood sugar values were less than 0.050 % — even as low as 0.038 % in the last ½ hour of the examination. No symptoms of hypoglycæmia was observed. In case No. 5 was found a hypoglycæmic value of 0.042 %. *On the whole, the alimentary blood sugar curves — before and after treatment — give normal findings in maximal values as well as in duration of the hyperglycæmia, just as found in normal children of the same age.*

Table 21.

Blood Sugar Curve in Children with Tetany.

(Before treatment: 6 children, aged 6—16 months; 10 examinations. After treatment: 3 children; 5 examinations. Dosage 2 gm. glucose per kg. of body weight).

	Before Treatment		After treatment	
	Average	Variations	Average	Variations
Fasting value % ...	0.069	0.045—0.077	0.076	0.069—0.090
Maximal value %	0.146	0.112—0.184	0.150	0.136—0.163
Rise of blood sugar %.	0.076	0.043—0.139	0.074	0.059—0.088
Time of maximal value after glucose ingest. in min.	43	10—105	26	15—40
Duration of hyperglycæmia in min.		80—120		60—120

Thus, my examinations of the alimentary hyperglycæmia in rickets and tetany give perfectly normal findings. In my material, tetany shows on the average no greater tendency to low blood sugar curves after glucose ingestion than does rickets. It should be added, however, that all these cases of tetany were complicated with rickets, and that this complication perhaps conceals a possible difference in the blood sugar regulation.

In tetany the fasting blood sugar values are generally very low — less than 0.070 %.) It may be that there is some connection between the altered electrolytic conditions of these children and their low fasting blood sugar values, or the difference in the blood sugar curve may be due to an increased consumption of glucose on account of the increased muscular activity. The normal course of the blood sugar curve after glucose ingestion demonstrates fully that there is no radical change in the blood sugar regulation.*

*) In subsequent examinations of the fasting blood sugar in 8 cases of tetany the results were:

Before treatment	After treatment
0.049	0.092
0.067	0.090
0.052	0.075
0.066	0.073
0.092	0.078
0.087	0.069
0.054	0.081
0.073	0.078
Average 0.069	0.080

Case Records of Rickets.

No. 1. — Girl. Reg. No. 353/1929. Born Nov. 19, 1928.

6 months.

Adm. May 23, 1929. Blood sugar exam. May 29 and 31.

Disch. July 25, 1929.

Born 4 weeks before full term. Weight at birth 2200 gm.

Diet: Mother's milk about 1 month; then milk mixtures. At the time of admission: Gruel, whole milk and rusk.

On adm.: Small, tiny, rather emaciated child. Signs of rickets: Craniotabes, rickety rosary, Harrison groove, epiphyseal swelling. Some perspiration of the head. Otherwise no abnormality on physical examination.

X-ray exam. June 29: Epiphyseal lines flossy and irregular, with tendency to normal growth.

Pt. treated with irradiated ergosterin (Vigantol), 10 drops a day. On this treatment she was improving, with return of good appetite.

After-exam. June 21, 1929: Cranium firm. Pt. capable of sitting without support. Still some epiphyseal swelling and rickety rosary. No sweating of the head. Pt. is bright and lively. Symptoms of rickets apparently subsiding.

X-ray exam. July 19: Healed rickets; sharp outlines of epiphysis.

Weight on adm. May 23, 1929: 5.750 kg.

» » disch. July 25, 1929: 7.000 »

+ 1.250 »

No. 2. — Boy. Reg. No. 297/1930. Born Nov. 5, 1929.

6 months.

Adm. May 15, 1930. Blood sugar exam. May 21 and 26.

Disch. June 6, 1930.

Born at full term. Diet: Mother's milk about 10 days; then milk mixtures. At the time of admission: Whole milk. Shortly before adm., pt. is somewhat weak. Loss of appetite. Subject to colds.

On adm.: Size and nutrition normal. Looks somewhat anæmic. Excessive perspiration of the head. Can hold up his head, but can not sit upright. Thorax flattened at the sides. Rickety rosary, everted curvatures, soft ribs. Sutures of the cranium resilient. Large fontanels. There is some dyspnoea, and hoarse râles are heard over both lungs. Otherwise no abnormality on physical examination. No rise of temperature.

Pt. treated with irradiated ergosterin (Ultranol) 10 drops a day, and Ferrum reductum, 25 gm. \times 2. On this treatment, he improved rapidly, and on discharge, his condition was considerably better.

Weight on adm. May 15, 1930: 6.830 kg.

» » disch. June 6, 1930: 7.000 »

+ 170 gm.

No. 3. — Boy. Reg. No. 466/1928. Born Febr. 15, 1928.

6 months.

Adm. Sept. 1, 1928. Blood sugar exam. Sept. 10.

Disch. Nov. 21, 1928.

Born 2 months before full term. Weight at birth 1700 gm. Diet: Mother's milk about 2 weeks; then milk mixtures. Some time before adm., subject to colds and perspiration. Otherwise, he has thrived well until then.

On adm.: Large, well-developed and well-nourished child. Can hold up his head, but can not sit upright without support, and is, on the whole, somewhat weak. Head large, typical Caput quadratum. Lumbar kyphosis, rickety rosary, pronounced Harrison groove, pronounced epiphyseal swelling. No teeth. There is some dyspnoea, and râles and rhonchi are heard over both lungs. No rise of temperature. On treatment with cod-liver oil, 5 gm. \times 2 daily, and later on with irradiated ergosterin (Vigantol), 10 drops once a day, the patient improved, and on discharge, the symptoms of rickets had greatly decreased.

Weight on adm. Sept. 1, 1928: 6.440 kg.

» » disch. Nov. 21, 1928: 7.290 »

+ 850 gm.

No. 4. — Girl. Reg. No. 123/1930. Born June 17, 1929.

7 months.

Adm. Febr. 7, 1930. Blood sugar exam. Febr. 8 and 13.

Disch. March 11, 1930.

Born about 1 month before full term. Weight at birth 2000 gm. Diet: Mother's milk a couple of weeks; then milk mixtures. At the time of adm.: Whole milk, gruel and crackers.

On adm.: Large, rather fat child. Turgor of the skin fairly good. Sutures of the cranium resilient. Epiphyseal swelling, Harrison groove, pronounced rickety rosary, lumbar kyphosis. No teeth. She is rather weak, can not sit upright. Pt. treated with irradiated ergosterin (Ultranol), 10 drops daily. After that marked improvement.

Weight on adm. Febr. 7, 1930: 7.160 kg.

» » disch. March 11, 1930: 7.140 »
÷ 20 gm.

No. 5. — Boy, Reg. No. 132/1930. Born July 1, 1929.

$\frac{7}{2}$ months.

Adm. Febr. 6, 1930. Blood sugar exam. Febr. 14.

Disch. March 16, 1930.

Pt. was born at full term, by natural delivery. Diet: No mother's milk, but milk mixtures until about 3 months old; then gruel and whole milk. One month before adm., he ceased trying to stand on his legs. Simultaneously, there was some soreness of the bones. Subject to colds.

On adm.: Rather fat and large child. Turgor of the skin fairly good. He is weak, can neither sit upright nor hold up his head. Considerable degree of craniotabes, almost parchment-like bones, sutures wide apart, square fontanel 4.5×5 cm., great soreness on palpation of the cranium, pronounced rickety rosary and Harrison groove, outstanding curvatures, curved legs. Epiphyseal swelling, soreness of the bones of the extremities. No skin bleeding, no signs of tetany. Pt. was treated with irradiated ergosterin (Ultranol), 10 drops a day. On this treatment he was improving. Examination after treatment for one month: Cranium almost firm, ribs firm. He can now sit upright, and hold up his head.

Weight on adm. Febr. 6, 1930: 7.450 kg.

» » disch. March 16, 1930: 7.650 »
+ 200 gm.

Case Records of Tetany.

No. 1. — Girl. Reg. No. 70/1929. Born July 10, 1928.

1/2 year.

Adm. Jan. 9, 1929. Blood sugar exam. Jan. 10 and 11; Febr. 8 and 16.
Disch. Febr. 18, 1929.

Born at full term by natural delivery. Diet: Mother's milk about one month; then milk mixtures. One month before adm. jerks and gasping. No cramps.

On adm.: Pronounced rickets. Facial phenomenon. Trousseau's sign. Electrical exam.: Greatly increased irritability. (C.O.C. 2.5). Otherwise no abnormality on physical examination. Pt. treated with irradiated ergosterin (Vigantol), 10 drops a day. On this treatment he was rapidly improving, and in about 10 days, all signs of tetany had disappeared.

On discharge, the rickety changes were also rapidly improving. Electrical exam. for irritability one month after adm. showed normal conditions. (C. O. C. > 10).

Weight on adm. Jan. 9, 1929: 7.150 kg.

» » disch. Febr. 18, 1929: 7.000 »

÷ 150 gm.

No. 2. — Boy. Reg. No. 137/1930. Born June 2, 1929.

8 1/2 months.

Adm. Febr. 21, 1930. Blood sugar exam. Febr. 22 and 24.

Disch. March 18, 1930.

Born at full term, by natural delivery. Diet: No mother's milk, on account of mother's illness. Milk mixtures. One month before admission, whole milk and gruel. He was perfectly well until 6 days before admission, when he became somewhat restless, especially in the night. There were several spells of cramps before adm. Pt. was admitted from the policlinic of the department, where he had a typical attack of tetany with tonic and thereupon clonic cramps; very pronounced carpopedal spasms.

On adm.: Large, well-developed child, rather fat, subject to jerks. Facial phenomenon, Trousseau's sign. There were signs of rickets in the form of a pronounced rickety rosary, and epiphyseal swelling at the wrists. Electrical exam.: Somewhat increased irritability. (C.O.C. 4.5. Calcium given 7 hours before exam.). After some days' treatment with irradiated ergosterin (Ultranol), 10 drops a day, the symptoms of tetany subsided, and on discharge he was perfectly bright and normal.

Electrical exam. on discharge showed normal conditions of irritability. C.O.C. > 7.0).

Weight on adm. Febr. 21, 1930: 9.050 kg.

» » disch. March 18, 1930: 8.900 »

÷ 150 gm.

No. 3. — Boy. Reg. No. 291/1929. Born Aug. 31, 1928.

9 months.

Adm. May 26, 1929. Blood sugar exam. May 28 and 30; June 4 and 8.

Disch. June 9, 1929.

Born at full term, by natural delivery. Diet: Mother's milk about one month; then milk mixtures; the last two months before adm., whole milk. 2 months before adm., pt. showed signs of increased irritability in the form of jerks and restlessness. Before adm., an attack of tonic cramps.

On adm.: Healthy-looking child, apart from signs of rickets in the form of epiphyseal swelling, Harrison groove, everted curvatures. Facial phenomenon. Trousseau's sign. Electrical exam.: increased irritability. (C.O.C. 3.5). On treatment with irradiated ergosterin (Vigantol), 10 drops a day, rapidly improving. On discharge, no signs of tetany. Pt. has brightened up somewhat. Electrical exam. now shows normal conditions. (C.O.C. > 10).

Weight on adm. May 26, 1929: 7.280 kg.

» » disch. June 9, 1929: 6.900 «

÷ 380 gm.

No. 4. — Boy. Reg. No. 500/1928. Born March 3, 1928.

9 months.

Adm. Nov. 30, 1928. Blood sugar exam. Dec. 3.

Disch. Dec. 16, 1928.

Born at full term, by natural delivery. Diet: Mother's milk about 5 months; now whole milk and gruel. 5 days before adm., attack of cramps, during which he was completely stiff and unconscious, later on beginnings of attacks.

On adm.: Well-developed, well-nourished child. Some epiphyseal swelling at the wrists and rickety rosary. Facial phenomenon. Trousseau's sign. Gasping for breath when crying. No attack of cramps

while in hosp. On treatment with calcium, cod-liver oil and universal quartz light, pt. rapidly improved. Completely well on discharge.

Weight on adm. Nov. 30, 1928: 7.550 kg.

» » disch. Dec. 16, 1928: 7.410 »

÷ 140 gm.

No. 5. — Girl. Reg. No. 236/1929. Born June 20, 1928.

10 months.

Adm. April 30, 1929. Blood sugar exam. May 2 and 17.

Disch. May 18, 1929.

Born at full term, by natural delivery. Diet: Mother's milk about 3 months; then increasing milk mixtures; now whole milk, gruel and mashed potatoes. The last couple of months before adm., pt. was cross and restless; gasping for breath when crying. The day before adm., an attack of cramps, lasting 5 minutes, accompanied with tonic and clonic convulsions and unconsciousness. Similar attacks 3 times afterwards in the course of 24 hours.

On adm.: Large child, fairly well-nourished, with signs of rickets as rosary and frontal bosses. Facialis phenomenon. Peroneal phenomenon. Trousseau's sign. A most cautious inspection of the fauces gave rise to an attack of cramps lasting 2 minutes, with unconsciousness and laryngospasms. Electrical exam. shows markedly increased irritability (C.O.C. 2). Under treatment with calcium and universal quartz light, pt. improves rapidly. On discharge, she seems perfectly well, without any sign of tetany. (C.O.C. > 10).

Weight on adm. April 30, 1929: 8.250 kg.

» » disch. May 18, 1929: 7.550 »

÷ 700 gm.

No. 6. — Boy. Reg. No. 91/1929. Born Aug. 27, 1927.

1½ year.

Adm. Jan. 10, 1929. Blood sugar exam. Jan. 13 and 23.

Disch. March 4, 1929.

Born 6 weeks prematurely. Weight at birth 2.650 kg. Had mother's milk the first 1½ month. His present diet consists of whole milk, gruel, mashed potatoes, etc. Has always been well before. 5 days ago, sudden attack of universal tonic and clonic cramps, accompanied by unconsciousness. Since then, no cramps, but gasping for breath when crying.

On adm.: Large child, well-nourished. Looks somewhat anæmic;

hæmoglobin 65 %. Signs of rickets as rosary and epiphyseal swelling at the wrists. Marked facialis phenomenon. Peroneal phenomenon. Trousseau's sign. Marked gasping for breath when crying. Electrical exam. shows increased irritability (C.O.C. 3.5). On treatment with irradiated ergosterin (Vigantol) and calcium, pt. improves rapidly. After 10 days of treatment, there is no longer any symptom of tetany. Electrical exam. shows normal irritability (C.O.C. 15). On discharge, the boy is perfectly well.

Weight on adm. Jan. 10, 1929: 9.700 kg.

» » disch. March 4, 1929: 11.450 »

+ 1.750 »

GLYCOSURIA.

Additional Remarks.

The literature contains only a few reports on investigations into the relation between glycosuria and hyperglycæmia in infants. Gilchrist ³⁰ (1929) has studied this question in children ranging in age from 1½ to 12 years, and she finds a threshold value for glycosuria around 0.230 % in the majority of the children. She was able to give up to 11 gm. glucose per kg. of body weight without producing glycosuria. On the other hand, she also found that glycosuria appears now and then after such small doses as 1 gm. glucose per kg.

Systematic studies on the relation between hyperglycæmia and glycosuria on infants would require that these children were lying with a permanent catheter throughout the examination. Instead of this, the infants of my material were lying with a collecting bottle during the blood sugar examination; and the older children were told to void at certain intervals. As to the infants, often a part of the urine has been lost, and sometimes no urine has been collected at all. The amounts collected from these infants have varied from 6 to 80 cc. The collecting bottle is not removed till the blood sugar examination is discontinued.

The urine is examined with Almén's fluid (9 cc. urine to 1 cc. Almén's fluid, boiling period 2 minutes).

The urine gave reduction only in 3 cases. In one case, it was a normal child, aged 5 months, who had had a dose of 6 gm. glucose per kg. of body weight. Here the blood sugar concentration reached a maximal value of 0.250 %, and it stayed on values above 0.200 % for 80 minutes.

In one child, aged 7 months, who was suffering from eczema, one of the examinations with 2 gm. glucose per kg. gave a strong reduction (4 cc. urine — some urine lost). In this case, the blood sugar concentration reached a maximal value of 0.224 %, and it stayed on values above 0.200 % for $\frac{1}{2}$ hour. Finally, there was a cretin, aged 1 year, who had been under thyroid treatment for one month, in whom the blood sugar concentration after glucose ingestion (2 gm. per kg.) rose to 0.254 %, and stayed on values above 0.200 % for 65 minutes. In this case, 10 cc. urine was collected, and it gave a very marked reduction.

Apart from these cases, there were 9 normal infants, in whom the maximal blood sugar value was over 0.200 %, even up to 0.250 %, without any of them showing glycosuria (doses 2—10 gm. glucose per kg.). None of the new-born children or older children (Groups I and III) showed reduction; but in these children there was indeed only one case with a maximal value above 0.200 % and lasting only 5 minutes.

Amongst the sick children, there was one case of coeliac disease (No. 4), a child of 5 years, in whom one of the blood sugar examinations, glucose ingestion + adrenalin injection, gave a blood sugar rise as high as 0.224 %. Here the blood sugar concentration stayed on values above 0.200 % for a whole hour, and yet the urine gave no reduction. 84 cc. urine was collected.

As it was not possible to collect the urine in portions, there is a possibility that a small amount of glucose might have been eliminated without being noticed; and this, of course, is a considerable shortcoming in these examinations. For this reason, I shall not discuss them at length but merely point out that *in the 3 cases where the urine reduced the Almén fluid, the blood sugar concentration was on very high levels (maximal values: 0.224, 0.250, and 0.254 %), and blood sugar values above 0.200 % were observed for 30—80 minutes.*

SUMMARY.

I. BLOOD SUGAR IN NORMAL CHILDREN.

Technique.

The blood sugar determinations are made after the Hagedorn-Jensen method. The glucose is given in 10 % watery solution.

After the glucose ingestion — or, in some instances, after other administration — the blood samples are taken, as a rule, every 5 minutes during the first 1½ hour, then every 10 minutes during the next hour, the examination period lasting as a rule 2½ hours.

During the examination period, the children are kept under as uniform conditions as possible, with regard to the diet as well as to other conditions.

Fasting Blood Sugar.

In 11 new-born children, aged 4—14 days, 22 examinations show an average fasting value of 0.083 %.

In 26 infants, aged from 15 days to 1 year, 58 examinations show an average fasting value of 0.080 %.

In 22 children, from 1 to 13 years old, 43 examinations show an average fasting value of 0.088 %.

Thus, there seems to be a tendency to somewhat lower fasting values in infants than in adults, in the first 2 weeks of life as well as throughout the first year of life; after this time, however, the fasting values observed in the children correspond with the fasting values generally obtained in adults.

In 11 children, aged from 2 months to 7 years, who were beforehand fasting $3\frac{1}{2}$ —15 hours, 14 examinations of the fasting blood sugar curve are made, with an examination period of 2— $3\frac{1}{2}$ hours, and with blood samples being taken generally every 10 minutes. The results of these tests are:

1) The fasting blood sugar values are subject to variations which in general do not appear as sudden changes, but as low and broad waves, in which the blood sugar values generally stay within the limits of the normal fasting values.

2) It will depend on the phase — crest or bottom of the wave — in which a blood sample is taken, whether the fasting blood sugar value in the same individual is somewhat higher or lower from day to day.

3) Occasionally one will find a particularly great variation of the fasting blood sugar value, without any demonstrable cause.

Behaviour of Blood Sugar after Ingestion of Glucose.

1. New-born.

In the first week of life, the blood sugar curve after glucose ingestion (2 gm. per kg. of body weight) shows in general a smaller degree of hyperglycæmia than is observed in the second week of life, and in subsequent infancy. The duration of the hyperglycæmia is less than $2\frac{1}{2}$ hours as in adults and older infants and children (11 children examined).

2. Infants (from 15 days to 1 year).

a) Infants show, on repeated examinations of the same child, far greater variations on different days with regard to

the hyperglycæmia after glucose ingestion (2 gm. per kg. of body weight) than the variations observed in older children and in adults, although the living conditions of the infants during the examination period are as uniform as by any means practicable.

b) It is further found that blood sugar values above 0.200 % — even up to 0.250 % — are frequent in children under 1 year after ingestion of 2 gm. glucose per kg. of body weight in watery solution, after 6—6½ hours' fasting. The duration of the hyperglycæmia as a rule is less than 2½ hours (20 children examined).

3. Older Children (1—13 years).

Uniform hyperglycæmic curves on repeated examinations of the same individual on different days are not obtained in these older children either (1.5 gm. glucose per kg. of body weight), but still the variations are far less than observed in the infants. In the older children (between 1 and 13 years) the alimentary hyperglycæmia after glucose ingestion runs a course quite similar to that in adults. (22 children examined).

4. Comparative Examinations after Different Doses of Glucose.

6 children, 5 in the first year of life and 1 aged 3½ years, are examined as to the blood sugar curve after ingestion of 1 and 2 gm. glucose, respectively, per kg. of body weight. In 2 cases, additional examinations are made after ingestion of 4, 6, and 10 gm. glucose. 2—5 examinations have been made on each child. It is found that the maximal blood sugar value after the different doses may vary within the same limits. It appears, as if there is certainly an »acceleration« of the blood sugar assimilation in children but taking place at a somewhat higher blood sugar level — above 0.200 % — than is the case in adults.

5. Comparative Examinations after Ingestion of Glucose and Saccharose.

6 children, aged 1—8 months, have been examined as to the blood sugar curve after the respective ingestion of 2 gm. glucose and 2 gm. saccharose per kg. of body weight. It is found that in most instances the hyperglycæmia is somewhat greater after glucose than after saccharose. This is no established rule, however, as the reverse may be found, and also nearly identical values.

II. BLOOD SUGAR OF CHILDREN IN SOME DISEASES.

1. Coeliac disease.

Children with coeliac disease (5 children, from 2 to 10 years old) show an extraordinarily slight degree of hyperglycæmia after ingestion of glucose in doses of 1—2 gm. per kg. of body weight. This peculiarity of the blood sugar regulation in these children is found remarkably constant on examinations on different days, even at intervals of months or years. The »low blood sugar curve« after ingestion of glucose in the doses mentioned is therefore to be regarded as a valuable diagnostic sign of coeliac disease.

In 5 infants with chronic dyspepsia, in whom the stools were voluminous and fatty, the hyperglycæmic curve after glucose ingestion showed no abnormality.

2. Cretinism.

In cretins (4 children, from 1 to 4 years old) the blood sugar curve after glucose ingestion (1.5—2 gm. per kg. of body

weight) shows a rather low rise, but not lower than encountered now and then in normal children of the same age. After thyroid treatment for some time, the same dose of glucose gives a marked hyperglycæmia. Thus, the thyroid treatment seems to have a powerful effect on the blood sugar regulation in cretins.

3. *Eczema (exudative diathesis).*

5 children suffering from exudative diathesis with eczema are examined as to the blood sugar curve after ingestion of 2 gm. glucose per kg. of body weight. These children show maximal values above 0.200 % perhaps somewhat more frequently than do normal children. Still, the blood sugar values do not exceed the findings often obtained after the same dose of glucose in normal children. The high maximal values do not appear to be associated with any limited duration of the skin eruption (less than 2 weeks, as asserted by Herlitz).

4. *Rickets.*

5 children, aged 6—8 months, with a marked degree of rickets, are examined as to the blood sugar curve after ingestion of 2 gm. glucose per kg. of body weight. In these children, the hyperglycæmic curve does not differ in any way from the findings obtained in normal children of the same age.

5. *Tetany.*

6 children with manifest tetany are examined as to the blood sugar curve after ingestion of 2 gm. of glucose per kg. of body weight. 4 of these children are examined during the presence of the symptoms as well as after the symptoms have

subsided. In these children, the hyperglycæmic curve does not differ from the findings in normal children of the same age.

During the manifest period of tetany, on the other hand, the fasting values were found to be lower than normal, the average fasting value being 0.069 %, with variations 0.045—0.077 %. After the symptoms have disappeared, the average fasting value is 0.076 %, and the variations 0.069—0.090 %.

RÉSUMÉ

I. BLODSUKKERETS FORHOLD HOS SUNDE BØRN.

Teknik.

Til Undersøgelserne er anvendt Hagedorn-Jensens Metode. Glykose er givet i 10 % vandig Opløsning.

Efter Glykoseindgift eller eventuel anden Belastning er der i Reglen taget Blodprøve hvert 5te Minut i de første halvanden Time, dernæst hvert 10ende Minut i den følgende Time, idet Undersøgelsens Varighed i Reglen har været $2\frac{1}{2}$ Time.

Børnene er i Undersøgelsesperioden med Hensyn til Kost og øvrige Levevis holdt paa saa ensartede Betingelser som overhovedet muligt.

Fasteundersøgelser.

Hos 11 nyfødte Børn i Alderen fra 4—14 Dage findes ved 22 Undersøgelser en Middelfasteværdi paa 0.083 %.

Hos 26 spæde Børn i Alderen fra 15 Dage til 1 Aar findes ved 58 Undersøgelser en Middelfasteværdi paa 0.080 %.

Hos 22 større Børn, 1 til 13 Aar gamle, findes ved 43 Undersøgelser en Middelfasteværdi paa 0.088 %.

Der synes saaledes at være en Tendens til noget lavere Fasteværdier end hos Voksne, saavel i de to første Leveuger som i hele det første Leveaar, medens Fasteværdierne for større Børns Vedkommende svarer til de Fasteværdier, der i Almindelighed findes hos Voksne.

Af 14 Undersøgelser paa 11 Børn i Alderen fra 2 Maaneder til 7 Aar efter en forudgaaende Fastetid paa $3\frac{1}{2}$ —15 Timer og med en Undersøgelsesvarighed af 2— $3\frac{1}{2}$ Time med gennemsnitlig Blodprøvetagning hvert 10ende Min. ses det:

1) Fastebloodsukkerværdierne er underkastet Variationer, der i Almindelighed ikke giver sig Udslag i bratte Udsving, men i et jævnt, langstrakt, bølgeformet Forløb, under hvilket Blodsukkeret holder sig indenfor de Grænser, der almindeligt findes for Fasteværdier.

2) Det vil afhænge af i hvilken Fase — Bølgetop eller Bølgedal — en Blodprøve bliver taget, om en Fastebloodsukkerværdi hos samme Individ fra den ene Dag til den anden findes noget højere eller lavere.

3) Undertiden findes uden paaviselig Aarsag et særlig højt Udsving af Fastebloodsukkeret.

Blodsukkerets Forhold efter Glykoseindgift pr. os.

1. Nyfødte Børn.

I første Leveuge frembyder Blodsukkerkurven efter Glykoseindgift (2 gr. pr. kg. Lgv.) gennemgaaende en ringere Hyperglykæmi end allerede i anden Leveuge og den senere Spædbarnsalder. Hyperglykæmiens Varighed er ligesom hos voksne og større Børn i Reglen mindre end $2\frac{1}{2}$ Time.

2. Spæde Born (15 Dage til 1 Aar).

a) Hos spæde Børn i første Leveaar ses der ved gentagne Undersøgelser hos samme Barn langt større Variationer paa forskellige Dage med Hensyn til den alimentære hyperglykæmiske Reaktion efter Glykoseindgift (2 gr. pr. kg. Lgv.), end man træffer hos større Børn og Voksne, endskønt de spæde Børns Levevis i Undersøgelsesperioden er saa ensartet, som det overhovedet er muligt.

b) Det findes endvidere, at Blodsukkerværdier over 0.200 % — helt op til 0.250 % — er hyppige hos Børn under 1 Aar ved Indgift af 2 gr. Glykose pr. kg. Lgv. i 10 % vandig Opløsning efter 6—6½ Times Faste. Hyperglykæmiens Varighed er i Reglen mindre end 2½ Time. (20 Børn undersøgt).

3. Større Børn (1—13 Aar).

Heller ikke hos større Børn opnaas indbyrdes ens hyperglykæmiske Kurver ved gentagne Undersøgelser paa forskellige Dage (1,5 gr. Glykose pr. kg. Lgv.), men Variationerne er dog langt mindre, end Tilfældet er for spæde Børns Vedkommende. Den alimentære Hyperglykæmi hos større Børn mellem 1 og 13 Aar efter Glykoseindgift forløber paa lignende Maade som hos Voksne. (22 Børn undersøgt).

4. Sammenlignende Undersøgelser efter forskellige Glykosedoser.

6 Børn, hvoraf 5 i første Leveaar og eet 3½ Aar gammelt, er undersøgt efter Indgift henholdsvis af 1 og 2 gr. Glykose pr. kg. Lgv. I 2 Tilfælde er der undersøgt ogsaa efter 4—6 og 10 gr. Glykose. Der er foretaget fra 2 til 5 Undersøgelser hos samme Barn. Det ses, at Blodsukkerets Maximalværdi efter alle Dosisstørrelser kan variere indenfor de samme Grænser. Det synes som om der ganske vist indtræder en »Acceleration« af Blodsukkerassimilationen hos Børn, men ved en noget højere Blodsukkerværdi — over 0.200 % — end hos Voksne.

5. Sammenlignende Undersøgelser efter Indgift af Glykose og Saccharose.

6 Børn i Alderen 1—8 Maaneder er blevet undersøgt med henholdsvis 2 gr. Glykose og 2 gr. Saccharose pr. kg. Lgv. Det

ses, at Hyperglykæmien som oftest bliver noget større efter Glykose end efter Saccharose; dette er dog ikke nogen fast Regel, idet man baade kan træffe det omvendte Forhold og næsten ens Værdier.

II. SYGE BØRN.

1. *Morbus coeliacus.*

Hos Børn med Morbus coeliacus (5 Patienter fra 2 — til 10 Aar gamle) er der fundet en overordentlig ringe Hyperglykæmi efter Glykoseindgift i Doser paa 1—2 gr. pr. kg. Lgv. Denne Ejendommelighed ved disse Børns Blodsukkerregulation optræder overordentlig konstant ved Undersøgelser paa forskellige Dage, endogsaa med Maaneders og Aars Mellemrum. Den »lave Blodsukkerkurve« efter den nævnte Glykosedosis maa derfor anses for at være et diagnostisk værdifuldt Symptom ved Mb. coeliacus.

Hos 5 Børn i første Leveaar med kroniske Dyspepsier, hos hvilke der fandtes voluminøse og fedtede Afføringer, frembød den hyperglykæmiske Kurve efter Glykoseindgift intet abnormt.

2. *Myxodema congenitum.*

Hos Børn med Myxodema congenitum (4 Tilfælde i Alderen fra 1 til 4 Aar) udviser Blodsukkerkurven efter Indgift af Glykose (1,5—2 gr. pr. kg. Lgv.) ret lav Stigning, dog ikke lavere end man jævnlig træffer det hos normale Børn i samme Aldersklasse. Efter nogen Tids Behandling med Thyreoidin kommer der en stærk Hyperglykæmi efter samme Glykosedosis. Behandlingen med Thyreoidin synes saaledes at have en kraftig Indvirkning paa Blodsukkerregulationen hos Børn med Myxodema congenitum.

3. Ekzema (*Exsudativ Diathese*).

Ved Undersøgelse af 5 Børn lidende af Ekzem (*Exsudativ Diathese*) med en Dosis af 2 gr. Glykose pr. kg. Lgv. findes muligvis noget hyppigere end ellers Maximalværdier over 0.200 %, men Værdierne overskrider dog ikke, hvad man ofte finder efter samme Glykosedosis hos normale Børn. De høje Maximalværdier synes ikke at være bundet til en bestemt Alder for Udslettet (mindre end 2 Uger, saaledes som hævdet af *Herlitz*).

4. *Rachitis*.

5 Børn i Alderen 6—8 Maaneder med florid *Rachitis* blev undersøgt med en Dosis af 2 gr. Glykose pr. kg. Lgv. Den hyperglykæmiske Kurve afveg ikke fra, hvad der blev fundet hos normale Børn i samme Aldersklasse.

5. *Tetania*.

6 Børn med manifest Tetani blev undersøgt med en Dosis af 2 gr. Glykose pr. kg. Lgv. 4 af disse Børn blev undersøgt saavel mens der var Symptomer til Stede som efter at disse var svundne. Den hyperglykæmiske Kurve afveg ikke fra, hvad der er fundet hos normale Børn i samme Aldersklasse.

Derimod fandtes i den manifest tetaniske Periode lavere Fasteværdier end normalt, idet Gennemsnittet for Fasteværdierne var 0.069 % med 0.045—0.077 % som Yderværdier. Efter at Symptomerne var svundne, fandtes en Middelfasteværdi paa 0.076 % med 0.069—0.090 % som Yderværdier.

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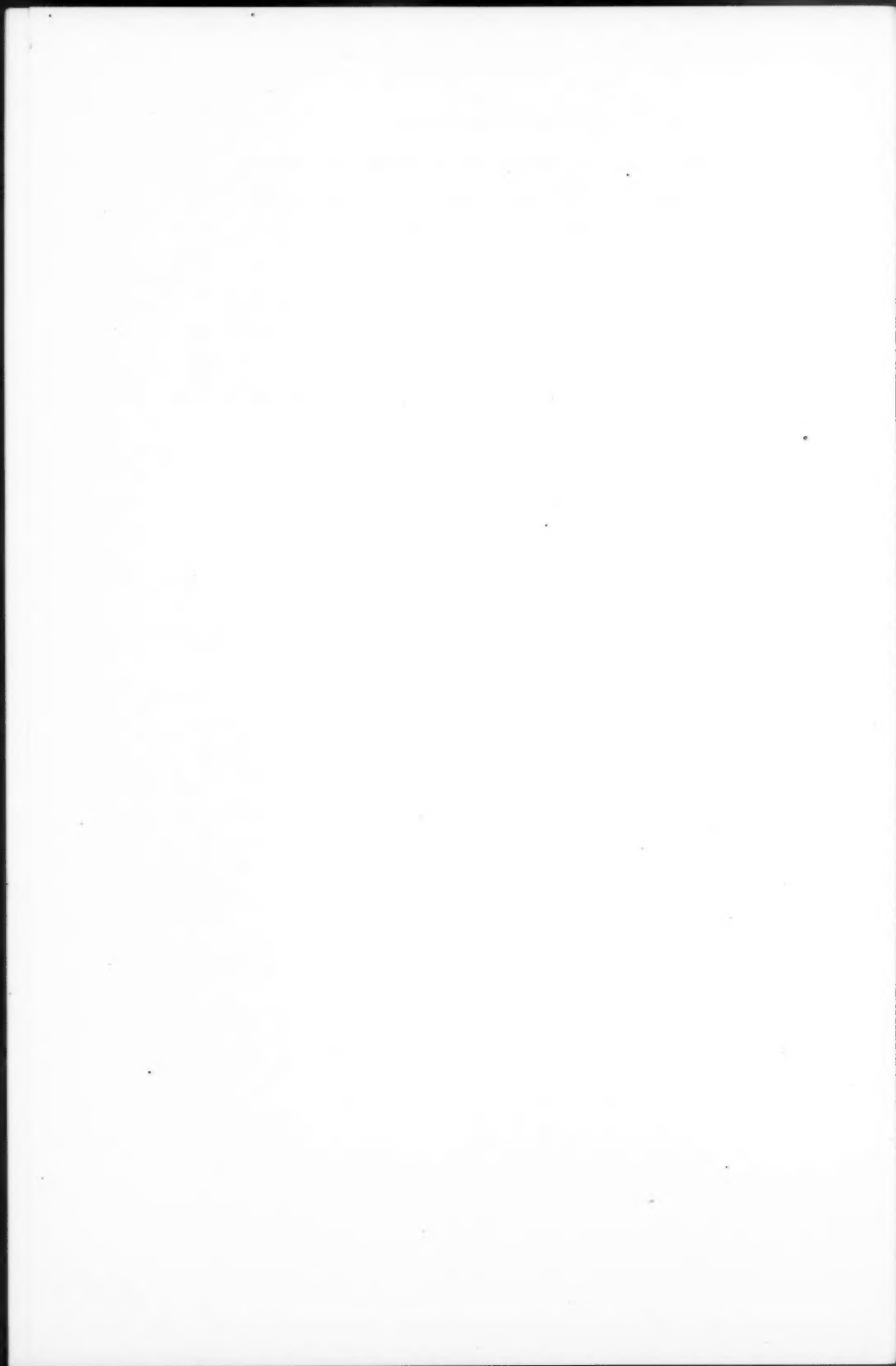
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PROTOCOLS
OF
BLOOD SUGAR VALUES



Fasting.

No. 1 (female).			No. 2 (male).	
Date	April 24, 1930	April 28	April 15, 1930	
Age	2 m. 15 d.	2 m. 19 d.	3 m. 16 d.	
Weight	3.650 kg.		5.050 kg.	
Diet	2 M + 1 B 150 cc. × 7	Same diet	2 M + 3 B 125 cc. × 7	
Fast. period. before exam.	3½ hours	3½ hours	3½ hours	
0 Min.	0.067	0.068	0 Min.	0.088
2 »	0.073	0.073	2 »	0.087
10 »	0.083	0.075	15 »	0.088
12 »	0.083	0.072	17 »	0.094
20 »	0.087	0.079	30 »	0.090
22 »	0.085	0.079	32 »	0.090
30 »	0.091	0.084	45 »	0.090
32 »	0.091	0.081	47 »	0.087
40 »	0.089	0.082	60 »	0.090
42 »	0.092	0.082	62 »	0.090
50 »	0.092	0.082	75 »	0.083
52 »	0.089	0.082	77 »	0.085
60 »	0.091	0.082	90 »	0.087
62 »	0.089	0.082	92 »	0.088
70 »	0.094	0.081	105 »	0.090
72 »	0.094	0.082	107 »	0.096
80 »	0.135	0.084	120 »	0.088
82 »	0.138	0.088	122 »	0.090
90 »	0.124	0.084	135 »	0.088
92 »	0.119	0.084	137 »	0.087
100 »	0.112	0.081	150 »	0.088
102 »	0.112	0.082	152 »	—
110 »	0.103	0.082	165 »	0.088
112 »	0.091	0.088	167 »	0.083
120 »	0.094	0.090	180 »	0.087
122 »	0.094	0.088	182 »	0.087
130 »	0.094	0.090		
132 »	0.101	0.090		
140 »	0.100	0.090		
142 »	0.094	0.090		
150 »	0.094	0.082		
152 »	0.094	0.082		
160 »	0.089	0.082		
162 »	0.087	0.086		
170 »	—	0.093		
172 »	—	0.090		
180 »	0.100	—		
182 »	0.101			
190 »	—			

Fasting.

No. 3 (male)			No. 4 (female)	No. 5 (female)	
Date	April 4, 1930	April 12	Nov. 20, 1930	April 5, 1930	
Age	4 m. 1 d.	4 m. 9 d.	6 m. 15 d.	6 m. 24 d.	
Weight	5.260 kg.		7.100 kg.	5.300 kg.	
Diet	3 M + 1 B 150 cc. × 4. Bum G. 150 cc. × 3.	Same diet	M 225 cc. × 2 G 225 " × 2 Omg 225 cc. × 1	2 M + 1 B 125 cc. × 7	
Fast. period. before exam.	3½ hours	3½ hours	6½ hours	3¼ hours	
0 Min.	0.080	0.070	0.090	0 Min.	0.076
10 »	0.086	0.072	0.090	10 »	0.074
20 »	0.088	0.072	—	20 »	0.077
30 »	0.086	0.072	0.097	30 »	0.067
40 »	0.086	0.068	0.099	40 »	0.072
50 »	0.092	0.072	0.099	50 »	0.074
60 »	0.088	0.068	0.099	60 »	0.079
70 »	0.085	0.065	0.096	70 »	0.079
80 »	0.070	0.070	0.094	80 »	0.076
90 »	0.092	0.065	0.090	90 »	0.074
100 »	0.081	0.070	0.088	105 »	0.076
110 »	0.079	—	0.094	120 »	0.076
120 »	0.081	—	0.096	135 »	0.076
130 »	0.083	—	—	150 »	0.076
140 »	0.081	—	—	165 »	0.070
150 »	0.070	0.072	—	180 »	0.076
160 »	—	0.074	—	195 »	0.070
170 »	—	0.070	—	210 »	0.070
180 »	—	0.068	—	225 »	0.070
190 »	—	—	—	240 »	0.076

Fasting.

No. 6 (male).			No. 7 (male).	No. 8 (male).
Date	March 14, 1930	March 19	Nov. 19, 1930	Nov. 22, 1930
Age	8 m. 12 d.	8 m. 17 d.	11 m. 21 d.	3 y 3 m.
Weight	6.300 kg.		8.650 kg.	14.700 kg.
Diet	M 225 cc. \times 2 G 225 " " 2 Omg 225 " " 1	Same diet	M 225 cc. \times 2 G 225 " " 2 Omg 225 " " 1	Ord. diet
Fast. period before exam.	6 hours	4 hours	6 $\frac{1}{2}$ hours	6 $\frac{1}{2}$ hours
0 Min.	0.081	0.079	0.091	0.088
10 "	0.081	0.080	0.084	0.096
20 "	0.081	0.080	0.086	0.085
30 "	0.082	0.078	0.084	0.087
40 "	0.081	0.089	0.086	0.092
50 "	0.079	0.078	0.086	0.094
60 "	0.081	0.081	0.091	0.087
70 "	0.082	0.076	0.096	0.099
80 "	0.081	0.071	0.089	0.092
90 "	0.081	0.071	0.087	0.088
100 "	0.086	0.072	0.086	0.085
110 "	0.084	0.074	0.086	0.085
120 "	0.086	0.071	0.086	0.088
130 "		0.074		
140 "		0.080		
150 "		0.080		
160 "		0.076		
170 "		—		
180 "		0.072		

Fasting.

No. 9 (female)		No. 10 (female)	No. 11 (male)
Date	Sept. 17, 1930	Sept. 20, 1930.	Oct. 3, 1930
Age	3 years	4 years	7 years
Weight	15. 100 kg.	19.600 kg.	20 kg.
Diet	Ord. diet	Ord. diet	Ord. diet
Fast. period before exam.	15 hours	15 hours	15 hours
0 Min.	0.105	0.101	0.101
2 »	0.105	0.098	—
10 »	0.105	0.094	0.101
12 »	0.105	0.092	—
20 »	0.100	0.092	0.101
22 »	0.100	0.091	0.101
30 »	0.095	0.094	0.094
32 »	0.095	0.092	—
40 »	0.102	0.091	0.099
42 »	0.095	0.096	0.094
50 »	0.097	0.091	0.092
52 »	0.100	—	—
60 »	0.099	0.091	—
62 »	0.102	0.089	0.094
70 »	0.104	0.087	0.094
72 »	0.104	0.092	0.094
80 »	0.097	0.092	0.092
82 »	0.097	0.092	0.094
90 »	0.097	0.091	0.092
92 »	0.091	0.094	0.094
100 »	0.091	0.089	0.096
102 »	0.098	0.092	0.092
110 »	0.095	0.091	0.088
112 »	0.099	0.092	0.099
120 »	0.097	0.092	0.094
122 »	0.097		0.094

Group I.

No. 1 (male)			No. 2 (male)		No. 3 (male)
Date	Jan. 29, 1930	Feb. 4, 1930	Feb. 1, 1930	Feb. 6, 1930	Feb. 12, 1930
Age	8 days	13 days	8 days	13 days	7 days
Weight	3.5 kg.	3.770 kg.	3.400 kg.	3.480 kg.	2.950 kg.
Birth wt.	3.350 kg.		3.200 kg.		3.050 kg.
Diet	Breast	Breast	Breast	Breast	Breast
Fasting period	5 hours	5½ hours	5 hours	5 hours	5 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	1 min.	1 min.	1 min.	2 min.	1 min.
Fasting bl. s. %	0.068	0.066	0.078	0.082	0.087
0 Min.	0.069	0.075	0.077	0.080	0.078
5 »	0.062	0.083	0.077	0.087	0.077
10 »	0.067	0.103	0.077	0.098	0.107
15 »	0.069	0.103	0.096	0.101	0.123
20 »	0.069	0.108	0.088	0.108	0.123
25 »	0.067	0.126	0.091	0.112	0.128
30 »	0.071	0.156	0.102	0.119	0.135
35 »	0.069	0.144	0.108	0.128	0.140
40 »	0.073	0.151	0.113	0.133	0.151
45 »	0.069	0.151	0.114	0.131	0.142
50 »	0.071	0.165	0.113	0.136	0.137
55 »	0.073		0.120	0.140	0.128
60 »		0.169	0.121	0.154	0.112
65 »	0.082	0.176	0.114	0.136	0.105
70 »	0.082	0.158	0.125	0.127	0.104
75 »	0.082	0.149	0.114	0.127	0.098
80 »	0.082	0.147	0.120	0.119	0.096
85 »	0.075	0.124	0.120	0.119	0.089
90 »	0.076	0.133	0.116	0.122	0.086
100 »	0.073	0.117	0.118	0.115	0.075
110 »	0.076	0.089	0.118	0.110	0.075
120 »	0.075	0.067	0.116	0.115	0.075
130 »	0.073	0.055	0.113	0.090	0.075
140 »	0.075	0.053	0.114	0.087	0.078
150 »	0.078	0.048	0.100	0.080	0.082

Group I.

No. 3 (male)		No. 4 (male)		No. 5 (female)	
Date	Feb. 18, 1930	Feb. 19, 1930	Feb. 25, 1930	March 3, 1930	March 11, 1930
Age	13 days	7 days	13 days	6 days	14 days
Weight	3.000 kg.	3.650 kg.	3.650 kg.	3.300 kg.	3.400 kg.
Birth wt.		3.650 kg.		3.450 kg.	
Diet	Breast	Breast	Breast	Breast	Breast
Fasting Period	5½ hours	5½ hours	5 hours	5 hours	5 hours
Glukose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	1 min.	2 min	1 min.	½ min.	1 min.
Fasting bl. s. $\frac{v}{10}$	0.081	0.082	0.078	0.097	0.099
0 Min.	0.080	0.084	0.092	0.097	0.094
5 »	0.110	0.104	0.113	0.106	0.101
10 »	0.133	0.109	0.115	0.117	0.107
15 »	0.142	0.123	0.124	0.129	0.103
20 »	0.145	0.123	0.126	0.132	0.120
25 »	0.144	0.130	0.134	0.140	0.117
30 »	0.127	0.117	0.134	0.140	0.126
35 »	0.127	0.123	0.136	0.150	0.124
40 »	0.133	0.124	0.129	0.150	0.140
45 »	0.149	0.124	0.143	0.149	0.131
50 »	0.147	0.116	0.140	0.145	0.134
55 »	0.160	0.119	0.141	0.149	0.134
60 »	0.151	0.116	0.140	0.149	0.145
65 »	0.144		0.140	0.149	0.151
70 »	0.135	0.107	0.127	0.141	0.131
75 »	0.117	0.100	0.124	0.131	0.131
80 »	0.120	0.105	0.122	0.124	0.127
85 »	0.115	0.095		0.127	0.113
90 »	0.106	0.077	0.115	0.124	0.113
100 »	0.091	0.060	0.101	0.099	0.089
110 »	0.071	0.059	0.090	0.103	0.074
120 »	0.064	0.051	0.085	0.098	0.067
130 »	0.076	0.039	0.099	0.074	0.074
140 »	0.069	0.048	0.099	0.074	0.074
150 »	0.076	0.053	0.090	0.075	0.081

Group I.

No. 6 (male)			No. 7 (male)		No. 8 (female)	
Date	Mar. 18, 30	Mar. 27, 30	Mar. 24, 30	Mar. 31, 30	Apr. 30, 30	May 5, 30
Age	5 days	14 days	4 days	11 days	7 days	12 days
Weight	3.300 kg.	3.600 kg.	3.500 kg.	3.600 kg.	3.850 kg.	3.900 kg.
Birth wt.	3.350 kg.		3.500 kg.		3.800 kg.	
Diet	Breast	Breast	Breast	Breast	Breast	Breast
Fasting period	5 hours	5 hours	5 hours	5 hours	5 hours	5 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	1 min.	1 min.	1 min.	1 min.	1 min.	1 min.
Fasting bl. s. $\frac{0}{100}$	0.077	0.089	0.073	0.080	0.086	0.079
0 Min.	0.078	0.087	0.089	0.091	0.093	0.090
5 »	0.079	0.120	0.089	0.095	0.100	0.111
10 »	0.083	0.132	0.094	0.091	0.100	0.114
15 »	0.087	0.134	0.092	0.098	0.111	0.143
20 »	0.088	0.147	0.092	0.116	0.132	0.144
25 »	0.105	0.147	0.108	0.117		0.164
30 »	0.103	0.141	0.105	0.119	0.143	0.170
35 »	0.115	0.147	0.105	0.133	0.146	0.179
40 »	0.097	0.139	0.110	0.123	0.143	0.191
45 »	0.097	0.147	0.108	0.123	0.148	0.166
50 »	0.108	0.143	0.108	0.128	0.143	0.157
55 »	0.108	0.138	0.107	0.116	0.139	0.171
60 »	0.094	0.123	0.110	0.139	0.141	0.173
65 »	0.094	0.123	0.112	0.144	0.143	0.182
70 »	0.087	0.122	0.120	0.131	0.139	0.186
75 »	0.094	0.111	0.119	0.123	0.137	0.179
80 »	0.094	0.111	0.115	0.130	0.141	0.164
85 »	0.087	0.109	0.115	0.123	0.132	0.170
90 »	0.087	0.090	0.110	0.109	0.143	
100 »	0.083	0.072	0.108	0.114	0.137	0.152
110 »	0.076	0.070	0.087	0.102	0.128	0.130
120 »	0.072		0.078	0.091	0.105	0.118
130 »	0.069	0.072	0.078	0.093	0.091	0.090
140 »	0.063	0.070		0.100	0.082	0.099
150 »	0.065	0.076	0.072	0.082	0.081	0.079

Group I.

No. 9 (female)			No. 10 (male)		No. 11 (male)	
Date	May 19, 30	May 26, 30	Sep. 22, 30	Sep. 27, 30	Mar. 21, 30	Mar. 26, 30
Age	7 days	14 days	7 days	12 days	7 days	12 days
Weight	3.600 kg.	3.550 kg.	3.000 kg.	3.120 kg.	2.850 kg.	2.950 kg.
Birth wt.	3.600 kg.		2.950 kg.		2.750 kg.	
Diet	Breast	Breast	Breast	Breast	Breast	Breast
Fasting period	5½ hours	5½ hours	5½ hours	5½ hours	5 hours	5 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	1 min.	1 min.	1 min.	1 min.	1 min.	1 min.
Fasting bl. s. %	0.098	0.091	0.096	0.082	0.075	0.071
0 Min.	0.102	0.100	0.099	0.105		0.067
5 »	0.107	0.137	0.106	0.117	0.095	0.073
10 »	0.116	0.144		0.122	0.097	0.075
15 »		0.164	0.110	0.140	0.104	0.084
20 »	0.120	0.171	0.110	0.154	0.102	0.084
25 »	0.120	0.182	0.110	0.158	0.104	0.084
30 »	0.127	0.195	0.108	0.170	0.102	0.084
35 »	0.125	0.189	0.115	0.165	0.114	0.089
40 »	0.134	0.197	0.117	0.178	0.109	0.089
45 »	0.141	0.197	0.125	0.174	0.102	0.093
50 »	0.147	0.185	0.125	0.170	0.109	0.096
55 »	0.152	0.173	0.132	0.183	0.100	0.085
60 »	0.156	0.164	0.139	0.183	0.113	0.085
65 »	0.147	0.153	0.129		0.113	0.085
70 »	0.159	0.160	0.134		0.113	0.087
75 »	0.152	0.137	0.115	0.172	0.091	0.087
80 »	0.152	0.126	0.112	0.170	0.088	
85 »	0.141	0.124		0.169	0.088	0.082
90 »	0.139	0.114	0.117	0.152	0.077	0.082
100 »	0.120	0.110	0.110	0.136	0.070	0.087
110 »	0.102	0.082	0.106	0.117	0.070	0.085
120 »	0.079	0.080	0.092	0.099	0.073	0.082
130 »	0.067	0.080	0.083	0.081	0.090	0.082
140 »	0.076	0.093		0.076	0.093	0.078
150 »	0.072	0.093	0.092	0.080	0.082	0.071

Group II.

No. 1 (female)

Date	July 1, 1929	July 6, 1929	July 12, 1929	July 16, 1929	July 19, 1929
Age	15 days	20 days	26 days	30 days	33 days
Weight	3.410 kg.	3.400 kg.	3.500 kg.	3.600 kg.	3.600 kg.
Diet	2 M + 3 B 75 cc. \times 7	Same diet	2 M + 3 B 100 cc. \times 7	Same diet	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	1 gm.	1 gm.	20% sol. 6 gm.
Time for ingestion	2 min.	1 min.	1 min.	1 min.	8 min.
Fasting bl. s. %	0.067	0.072	0.085	0.074	0.074

0 Min.	0.075	0.082	0.087	0.079	0.104
5 »	0.089	—	0.098	0.094	—
10 »	0.096	0.105	0.116	0.104	0.159
15 »	—	0.112	—	0.104	—
20 »	0.100	0.138	0.116	0.104	—
25 »	0.100	0.122	0.117	0.108	0.165
30 »	0.100	0.124	0.126	0.108	0.159
35 »	0.100	0.119	0.133	0.118	0.140
40 »	0.089	0.124	0.130	0.108	0.147
45 »	0.091	0.128	0.130	0.108	0.143
50 »	0.094	0.131	0.123	0.111	—
55 »	0.093	0.131	0.112	0.111	0.140
60 »	0.096	0.124	0.112	0.096	—
65 »	0.100	0.124	—	0.085	0.132
70 »	0.110	0.114	0.109	0.079	0.122
75 »	—	0.114	0.098	—	—
80 »	0.102	0.117	0.095	0.079	0.109
85 »	0.103	0.105	0.095	0.079	—
90 »	0.103	0.107	0.087	0.079	0.115
100 »	0.105	0.100	0.095	0.094	0.099
110 »	0.100	0.093	0.102	0.090	0.092
120 »	0.093	0.089	0.091	0.083	0.096
130 »	0.089	0.093	0.086	0.085	0.092
140 »	0.089	0.094	0.087	0.078	0.087
150 »	0.094	0.089	0.091	0.076	0.092

Group II.

No. 2 (male)			No. 3 (male)		
Date	Jan. 31, 1930	Feb. 27, 1930	Oct. 1, 1928	Oct. 8, 1928	
Age	17 days	44 days	2 m. 4 d.	2 m. 11 d.	
Weight	3.350 kg.	3.840 kg.	4.940 kg.	5.070 kg.	
Diet	1 M + 2 B 75 cc. \times 7 + 6 % Sacch.	1 M + 1 B 150 cc. \times 7	1 M + 1 B 150 cc. \times 7	Same diet	
Fasting period	6 hours	6 hours	6 hours	6 hours	
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	
Time for ingestion	1 min.	1 min.	2 min.	2 min.	
Fasting bl. s %	0.078	0.075	0.074	0.070	
0 Min.	0.084	0.080	0 Min.	0.085	0.098
5 »	0.098	0.108	2 »	0.082	—
10 »	0.104	0.126	10 »	0.105	0.133
15 »	0.106	0.147	12 »	0.109	0.135
20 »	0.098	0.154	20 »	0.119	0.126
25 »	0.098	0.165	22 »	0.121	0.124
30 »	0.100	0.160	30 »	0.109	0.114
35 »	0.107	0.163	32 »	0.105	0.112
40 »	0.106	0.158	40 »	0.109	0.121
45 »	0.111	0.151	42 »	0.102	0.124
50 »	0.119	0.129	50 »	0.107	0.109
55 »	0.107	0.115	52 »	0.098	—
60 »	0.114	0.101	60 »	0.089	0.117
65 »	0.112	0.100	62 »	0.087	0.117
70 »	0.102	—	70 »	0.091	0.110
75 »	0.102	0.091	72 »	0.087	0.105
80 »	0.097	—	80 »	0.085	0.098
85 »	0.098	0.083	82 »	0.091	—
90 »	0.098	0.100	90 »	0.076	0.092
100 »	0.088	0.108	92 »	0.080	0.098
110 »	0.079	0.105	100 »	0.087	0.087
120 »	0.080	0.106	102 »	—	0.083
130 »	0.086	0.105	110 »	0.087	0.085
140 »	0.089	0.098	112 »	—	0.082
150 »	0.086	0.091	120 »	0.089	0.085
			122 »	0.087	0.082
			130 »	0.084	—
			140 »	0.084	—
			150 »	0.082	—

Group II.

No. 4 (male)		(No. 5 male)		No. 6 (female)	
Date	Feb. 2, 29	Dec. 21, 29	Dec. 23, 29	Sep. 4, 29	Sep. 10, 29
Age	2 m. 15 d.	2 m. 19 d.	2 m. 21 d.	2 m. 22 d.	2 m. 28 d.
Weight	6.400 kg.	4.310 kg.	4.325 kg.	3.550 kg.	3.675 kg.
Diet	2 M + 1 B 200 cc. × 5	2 M + 1 B 125 cc. × 7	Same diet	2 M + 1 B 125 cc. × 7	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	1 min.	2 min.
Fasting bl. s. $\frac{0}{100}$	0.080	0.078	0.087	0.067	0.082
0 Min.	0.092	0.096	0.105	0.071	0.090
5 »	0.117		0.126	0.098	0.111
10 »	0.127	0.134	0.125	0.107	0.130
15 »	0.152	0.152	0.134	0.133	0.141
20 »	0.161	0.149	0.144	0.133	0.132
25 »	0.161	0.151	0.153	—	0.150
30 »	0.151	0.151	0.175	0.133	0.136
35 »	0.133	0.147	0.171	—	0.118
40 »	0.124	0.143	0.175	0.102	—
45 »	0.107	0.154	0.175	0.084	0.116
50 »	0.096	—	0.186	0.077	—
55 »	0.096	0.151	0.166	0.062	0.097
60 »	0.089	0.151	0.166	0.059	0.100
65 »	0.096	0.147	0.164	0.061	0.079
70 »	0.087	0.147	0.157	0.064	0.079
75 »	0.092	0.145	0.150	0.070	0.088
80 »	0.096	0.142	0.125	0.070	0.072
85 »	0.090	0.134	0.126	0.070	0.079
90 »	0.087	0.136	0.107	0.079	0.072
100 »	0.081	0.124	0.092	0.088	0.079
110 »	0.081	0.113	0.077	0.052	—
120 »	0.081	0.103	0.064	0.052	0.070
130 »	0.089	0.085	0.054	0.059	0.079
140 »	0.085	0.081	0.072	0.062	0.074
150 »	0.083	0.078	0.075	0.073	0.063

Group II.

No. 7 (female)			No. 8 (male)		
Date	Jan. 30, 29	Feb. 1, 29	Oct. 5, 28	Oct. 9, 28	
Age	3 m. 26 d.	3 m. 28 d.	3 m. 5 d.	3 m. 9 d.	
Weight	4.240 kg.	4.240 kg.	5.770 kg.	5.980 kg.	
Diet	2 M + 1 B 125 cc. \times 7	Same diet	2 M + 1 B 150 cc. \times 7	Same diet	
Fasting period	6 hours	6 hours	6 hours	6 hours	
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	
Time for ingestion	2 min.	2 min.	2 min.	1 min.	
Fasting bl. s. %	0.073	0.084	0.082	0.073	
0 Min.	0.097	0.087	0 Min.	0.084	0.081
5 »	0.118	0.100	2 »	0.082	0.081
10 »	0.166	0.158	10 »	0.119	0.110
15 »	0.177	0.169	12 »	0.121	0.113
20 »	0.180	0.180	20 »	0.126	0.120
25 »	0.180	0.198	22 »	0.140	0.119
30 »	0.191	0.193	30 »	0.171	0.127
35 »	0.191	0.187	32 »	0.165	0.129
40 »	—	0.166	40 »	0.169	0.131
45 »	0.166	0.142	42 »	0.173	0.131
50 »	0.139	0.126	50 »	0.185	0.140
55 »	0.111	0.102	52 »	0.180	0.138
60 »	0.084	0.102	60 »	0.191	0.143
65 »	0.097	0.098	62 »	0.191	—
70 »	0.068	0.098	70 »	0.185	0.133
75 »	0.079	0.105	72 »	0.178	0.136
80 »	0.079	0.109	80 »		0.129
85 »	0.082	0.084	82 »	0.171	0.126
90 »	0.107	0.082	90 »	0.174	0.115
100 »	0.100	0.073	92 »	0.180	0.126
110 »	0.105	0.068	100 »	0.164	0.120
120 »	0.104	0.080	102 »	0.160	0.122
130 »	0.082	0.082	110 »	0.155	0.119
140 »	0.068	—	112 »	0.149	0.115
150 »	0.068	0.080	120 »	0.135	0.115
			122 »	0.130	0.117
			130 »	0.119	0.112
			132 »	0.123	0.107
			140 »	0.111	0.113
			142 »	0.109	0.105
			150 »	0.102	0.090
			152 »	0.102	—

Group II.

No. 9 (male)			No. 10 (male)		
Date	Oct. 31, 28	Nov. 7, 28	Apr. 16, 30	Apr. 22, 30	
Age	3 m. 5 d.	3 m. 12 d.	3 m. 16 d.	3 m. 22 d.	
Weight	4.870 kg.	5.000 kg.	5.050 kg.	5.230 kg.	
Diet	2 M + 1 B 225 cc. \times 5	Same diet	2 M + 1 B 125 cc. \times 7	Same diet	
Fasting period	6 hours	6 hours	6 hours	6 1/2 hours	
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	
Time for ingestion	2 min.	2 min.	2 min.	2 min.	
Fasting bl. s. %	0.088	0.067	0.086	0.090	
0 Min.	0.102	0.075	0 Min.	0.098	0.097
2 »	0.102	0.080	5 »	0.139	0.129
10 »	0.150	0.123	10 »	0.157	0.149
12 »	0.146	0.140	15 »	0.169	0.165
20 »	0.179	0.160	20 »	0.187	0.183
22 »	0.172	0.174	25 »	0.198	0.197
30 »	0.173	0.180	30 »	0.198	0.197
32 »	0.181	0.165	35 »	0.191	0.207
40 »	0.175	0.165	40 »	0.217	0.207
42 »	0.175	0.174	45 »	0.240	0.207
50 »	0.175	0.173	50 »	0.232	0.201
52 »	0.175	0.171	55 »	0.226	0.197
60 »	0.161	0.162	60 »	0.217	0.218
62 »	0.163	0.160	65 »	0.223	0.201
70 »	0.159	0.147	70 »	0.207	0.183
72 »	—	0.147	75 »	0.207	0.159
80 »	0.132	0.126	80 »	0.206	0.143
82 »	0.134	0.126	85 »	0.187	0.134
90 »	0.112	0.111	90 »	0.155	0.127
92 »	0.104	0.111	100 »	0.102	0.097
100 »	0.088	0.096	110 »	0.102	0.088
102 »	0.083	0.091	120 »	0.087	0.096
110 »	0.068	0.064	130 »	0.071	0.099
112 »	0.074	0.060	140 »	0.069	0.108
120 »	0.066	0.053	150 »	0.068	0.115
122 »	0.070	0.049			
130 »	0.079	0.058			
132 »	0.074	0.062			
140 »	0.075	0.082			
142 »	0.075	0.084			
150 »	0.079	0.085			
152 »	0.079	0.087			

Group II.

No. 11 (female)			No. 12 (male)	
Date	Sep. 3, 1929	Sep. 7, 1929	Dec. 30, 1929	Jan. 3, 1930
Age	3 m 17 d.	3 m. 21 d.	4 m. 8 d.	4 m. 12 d.
Weight	4.280 kg.	4.375 kg.	7.150 kg.	7.030 kg.
Diet	3 M + 1 B 125 cc. \times 7	Same diet	3 M + 1 B 150 cc. \times 7	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	1 min.
Fasting bl. s %	0.085	0.085	0.086	0.079
0 Min.	0.074	—	0.099	0.080
5 »	0.136	0.086	0.115	0.121
10 »	0.159	0.114	—	0.133
15 »	0.195	0.135	0.158	0.140
20 »	0.195	0.137	0.145	—
25 »	0.222	0.141	0.138	0.144
30 »	0.214	—	0.127	0.156
35 »	0.199	0.133	0.122	0.151
40 »	0.195	0.141	0.122	0.156
45 »	0.175	0.164	0.131	0.160
50 »	0.159	0.175	—	0.151
55 »	0.146	0.164	0.165	0.156
60 »	0.150	—	0.147	0.147
65 »	0.141	0.164	0.131	0.147
70 »	0.132	0.164	0.127	0.137
75 »	0.120	0.123	0.127	0.121
80 »	0.097	0.117	0.142	0.119
85 »	0.102	0.098	—	0.108
90 »	0.088	0.071	0.125	0.105
100 »	0.083	0.064	0.113	0.102
110 »	0.083	0.086	0.117	0.094
120 »	0.088	0.093	0.127	0.094
130 »	0.060	0.089	0.124	0.087
140 »	0.074	0.082	0.106	0.094
150 »	0.059	0.064	0.127	0.080
160 »				0.093
170 »				0.087
180 »				0.076

*Group II.***No. 13 (male)**

Date	Apr. 30, 29	May 4, 1929	May 10, 1929	May 14, 1929	May 23, 1929
Age	5 m. 24 d.	5 m. 28 d.	6 m. 4 d.	6 m. 8 d.	6 m. 17 d.
Weight	5.940 kg.	6.000 kg.	6.240 kg.	6.375 kg.	6.500 kg.
Diet	3 M + 1 B 200 cc. × 3 G 200 gm.	Same diet	Same diet	Same diet	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	4 gm.	6 gm.	20 % sol. 10 gm.
Time for ingestion	2 min.	2 min.	2 min.	3 min.	2 min.
Fasting bl. s. $\frac{g}{100}$	0.084	0.093	0.079	0.071	0.073

0 Min.	0.092	0.091	0.098	0.091	0.091
5 "	0.135	0.126	0.149	0.140	0.146
10 "	0.162	0.146	0.180	0.166	0.182
15 "	—	0.149	0.203	0.210	0.200
20 "	0.190	0.153	0.215	0.233	0.217
25 "	0.205	0.140	0.215	0.250	0.225
30 "	0.228	0.140	0.207	0.240	0.204
35 "	0.236	0.128	0.207	0.217	0.198
40 "	0.241	0.124	0.213	0.195	0.200
45 "	0.234	—	0.205	0.164	0.173
50 "	0.249	0.107	0.205	0.146	0.137
55 "	0.232	0.102	0.200	0.124	0.116
60 "	0.219	0.096	0.190	0.119	0.095
65 "	0.205	—	0.180	—	0.089
70 "	0.190	0.105	0.171	0.107	0.057
75 "	0.189	0.104	0.147	0.089	0.050
80 "	0.190	0.107	0.136	0.060	0.050
85 "	0.192	0.104	0.124	0.057	0.053
90 "	0.167	0.096	0.113	0.053	0.059
95 "	—	0.087	0.115	0.051	0.059
100 "	0.147	0.066	0.100	0.057	0.066
105 "	0.133	0.060	0.103	0.064	0.068
110 "	0.119	0.060	0.108	—	0.075
115 "	0.101	0.060	0.103	0.066	0.073
120 "	0.101	—	0.108	0.068	0.077
125 "	0.065	—	—	0.064	—
130 "	0.051	—	0.106	0.069	0.075
135 "	0.038	—	—	0.064	—
140 "	0.053	—	0.096	0.064	0.073
145 "	0.043	—	—	0.066	—
150 "	0.053	—	0.089	0.077	0.077

Group II.

No. 14 (male)			No. 15 (male)	
Date	Sep. 21, 1928	Sep. 25, 1928	Nov. 16, 1928	Nov. 20, 1928
Age	6 m. 23 d.	6 m. 27 d.	9 m. 3 d.	9 m. 7 d.
Weight	8.000 kg.	8.200 kg.	7.960 kg.	8.220 kg.
Diet	M 150 cc. \times 5 + 6 $\frac{0}{10}$ sugar G 150 gm. \times 2	Same diet	M 250 cc. \times 2 G 225 gm. \times 2 Omg 225 gm. + 1 zwieback	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min	2 min.	2 min.	2 min.
Fasting bl. s. $\frac{0}{10}$	0.081	0.090	0.081	0.084

0 Min.	0.101	0.103	0.085	0.103
2 »	0.105	—	0.090	0.113
10 »	0.143	0.147	0.179	0.165
12 »	0.149	0.149	—	0.174
20 »	0.142	0.156	0.188	0.190
22 »	0.138	0.159	0.181	0.197
30 »	0.149	0.163	—	0.195
32 »	0.143	0.167	—	0.202
40 »	0.090	0.159	0.183	0.202
42 »	0.092	0.158	0.185	0.205
50 »	0.096	0.154	0.181	0.192
52 »	—	—	0.158	0.195
60 »	0.101	0.149	0.133	0.183
62 »	0.107	0.141	0.131	0.183
70 »	0.106	0.141	0.105	0.170
72 »	0.106	0.143	0.087	—
80 »	0.101	0.131	0.067	0.131
82 »	0.105	0.127	0.065	0.131
90 »	0.099	0.127	0.051	0.083
92 »	0.105	0.127	0.054	0.081
100 »	0.090	0.112	0.078	0.049
102 »	0.094	0.108	0.079	0.049
110 »	0.094	0.105	0.090	0.045
112 »	0.094	0.101	0.092	0.054
120 »	0.090	0.090	0.096	0.081
122 »	0.090	—	0.096	0.092
130 »	0.095	0.110	0.092	0.092
132 »	0.092	0.106	0.096	0.095
140 »	0.090	0.127	0.096	0.077
142 »	0.083	0.129	0.096	0.076
150 »	0.087	0.103	0.076	0.076
152 »	0.092	0.114	0.074	0.076

Group II.

No. 16 (male)

Date	Nov. 9, 1928	Nov. 12, 1928	Nov. 19, 1928	Nov. 23, 1928
Age	9 m. 8 d.	9 m. 11 d.	9 m. 18 d.	9 m. 22 d.
Weight	8.800 kg.	8.700 kg.	8.950 kg.	9.000 kg.
Diet	3 M + 1 B 225 cc. × 7	Same diet	M 225 cc. × 2 G 225 gm. × 2 Omg. 225 gm. × 1	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	1 gm.	1 gm.
Time for ingestion	15 min.	5 min.	2 min.	2 min.
Fasting bl. s. %	0.079	0.084	0.071	0.078
0 Min.	0.087	0.081	0.080	0.078
2 »	0.091	0.079	0.078	0.083
10 »	0.109	0.129	0.091	0.083
12 »	0.131	0.131	0.089	—
20 »	0.166	0.141	0.087	0.114
22 »	0.160	0.143	0.087	0.115
30 »	0.162	0.166	0.114	0.128
32 »	0.167	0.163	0.124	0.131
40 »	0.166	0.170	0.124	0.138
42 »	—	0.170	0.103	—
50 »	0.173	0.175	0.103	0.142
52 »	0.173	0.175	0.092	0.136
60 »	0.167	0.184	0.080	0.121
62 »	0.166	0.175	0.080	0.121
70 »	0.155	0.161	0.085	0.112
72 »	0.160	0.156	0.083	0.109
80 »	0.157	0.148	0.105	0.089
82 »	0.155	0.138	0.105	0.085
90 »	0.140	0.110	0.101	0.085
92 »	0.135	0.110	0.101	0.082
100 »	0.112	0.117	0.083	0.094
102 »	0.109	0.113	0.080	0.092
110 »	0.107	—	0.078	0.096
112 »	0.100	—	0.082	0.091
120 »	0.073	0.101	0.074	0.082
122 »	0.073	0.099	0.080	0.083
130 »	0.066	0.077	0.074	0.065
132 »	—	—	0.078	0.065
140 »	0.068	0.076	0.080	0.073
142 »	—	—	0.082	0.069
150 »	0.057	0.070	0.080	0.078
152 »	0.060	0.070	0.082	0.073

Group II.

No. 17 (male)		No. 18 (male)	
Date	Feb. 5, 1929	May 3, 1930	May 9, 1930
Age	9 m. 13 d.	9 m. 22 d.	9 m. 28 d.
Weight	10.420 kg.	7.700 kg.	8.430 kg.
Diet	M 225 cc. \times 2 G 225 gm. \times 2 Omg. 225 gm. \times 1	M 225 cc. \times 2 G 225 gm. \times 2 Omg. 225 gm. \times 1	Same diet
Fasting period	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.
Time for ingestion	1 min.	2 min.	2 min.
Fasting bl. s. $\frac{g}{\%}$	0.101	0.083	0.089
0 Min.	0.100	0.102	0.102
5 »	0.132	0.142	0.123
10 »	0.135	0.157	0.159
15 »	0.135	0.187	0.175
20 »	0.153	0.210	0.191
25 »	0.164	0.218	0.195
30 »	0.179	0.225	0.225
35 »	0.171	—	0.229
40 »	0.193	0.186	0.229
45 »	0.191	0.171	0.237
50 »	0.189	0.155	0.240
55 »	0.193	0.135	0.250
60 »	0.201	0.128	0.246
65 »	0.189	0.117	0.238
70 »	0.159	0.116	0.238
75 »	0.148	0.117	0.244
80 »	0.146	0.124	0.235
85 »	0.111	0.133	0.242
90 »	0.084	0.135	0.237
100 »	0.081	0.117	0.218
110 »	0.075	0.116	0.175
120 »	0.100	0.116	0.135
130 »	0.118	0.112	0.097
140 »	0.109	0.116	0.098
150 »	0.102	0.102	0.105

Group II.

No. 19 (male)			No. 20 (male)	
Date	Dec. 5, 1928	Dec. 24, 1928	Nov. 29, 1928	Dec. 18, 1928
Age	11 m. 22 d.	12 m. 12 d.	11 m. 24 d.	12 m. 13 d.
Weight	9.230 kg.	9.300 kg.	6.600 kg.	7.000 kg.
Diet	M 225 cc. × 2 G 225 gm. × 2 Omg. 225 gm. × 1	Same diet	3 M + 1 B 225 cc. × 3 G 225 gm. × 2	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	2 min.
Fasting bl. s. $\frac{g}{\%}$	0.089	0.082	0.086	0.075
0 Min.	0.087	0.103	0.091	0.094
2 »	0.094	0.110	0.091	0.089
10 »	0.122	0.181	0.107	—
12 »	0.122	0.181	0.103	0.126
20 »	0.119	0.181	0.105	0.149
22 »	0.119	0.181	0.109	0.147
30 »	0.113	0.172	0.105	0.158
32 »	0.115	—	0.098	0.160
40 »	0.113	0.167	0.098	0.160
42 »	—	0.174	0.107	0.163
50 »	0.098	0.149	0.098	—
52 »	0.098	0.151	0.098	0.169
60 »	0.098	0.151	0.080	0.167
62 »	—	0.161	0.085	0.165
70 »	0.090	0.117	0.076	0.145
72 »	0.094	0.117	0.080	0.142
80 »	0.080	0.099	0.084	0.103
82 »	0.080	0.094	0.085	0.101
90 »	0.072	0.056	0.088	0.074
92 »	0.065	0.056	0.091	—
100 »	0.072	0.085	0.089	0.089
102 »	—	—	0.098	—
110 »	0.072	0.089	0.098	0.094
112 »	—	—	—	—
120 »	0.087	0.078	0.094	0.115
122 »	0.087	—	0.093	0.115
130 »	0.076	0.074	0.094	0.098
132 »	—	—	—	—
140 »	0.080	0.084	0.098	0.096
142 »	—	—	—	—
150 »	0.072	—	0.096	0.098
152 »	0.076	—	0.096	—

Group Iii.

No. 1 (male)			No. 2 (male)	
Date	Jan. 6, 1930	Jan. 9, 1930	Dec. 13, 1930	Dec. 17, 1930
Age	13 m. 5 d.	13 m. 8 d.	2 y. 6 m.	
Weight	8.300 kg.	8.400 kg.	11.100 kg.	11.300 kg.
Diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14 hours	14 hours	14½ hours	14½ hours
Glucose per kg. of b. w.	2 gm.	2 gm.	1.5 gm.	1.5 gm.
Time for ingestion	1 min.	1 min.	4 min.	3 min.
Fasting bl. s. $\frac{6}{9}$	0.085	0.078	0.068	0.085

0 Min.	0.090	0.099	0.072	0.087
5 »	0.135	0.111	0.074	0.085
10 »	0.135	0.128	0.086	0.103
15 »	0.128	0.128	0.097	0.105
20 »	0.125	0.121	0.104	0.126
25 »	0.123	0.119	0.110	0.126
30 »	0.121	0.116	0.112	0.129
35 »	0.118	0.114	0.115	0.129
40 »	0.116	0.105	0.118	0.139
45 »	0.102	0.107	0.118	0.142
50 »	0.107	0.104	0.122	0.134
55 »	0.112	0.100	0.124	0.142
60 »	0.105	0.091	0.120	0.127
65 »	0.100	0.090	0.117	0.126
70 »	0.090	0.090	0.113	0.120
75 »	0.086	0.086	0.131	0.117
80 »	0.081	0.084	0.141	0.108
85 »	0.081	0.077	0.127	0.107
90 »	0.079	0.075	0.131	0.094
100 »	0.082	0.079	0.122	0.099
110 »	0.077	0.084	0.115	0.101
120 »	0.082	0.075		0.092
130 »	0.079	0.077	0.090	0.076
140 »	0.075	0.077	0.085	0.062
150 »	0.075	0.073	0.074	0.062

Group III.

No. 3 (male)			No. 4 (female)	
Date	Dec. 11, 30	Dec. 15, 30	Dec. 12, 30	Dec. 16, 30
Age	2 y. 7½ m.		2 y. 9 m.	
Weight	17.000 kg.	17.000 kg.	12.300 kg.	12.900 kg.
Diet	Ord. diet	Ord. diet.	Ord. diet.	Ord. diet
Fasting period	14½ hours	14½ hours	14½ hours	14½ hours
Glucose per kg. of b. w.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.
Time for ingestion	6 min.	3 min.	5 min.	5 min.
Fasting bl. s. %	0.087	0.081	0.088	0.091
0 Min.	0.091	0.084	0.083	0.089
5 "	0.107	0.110	0.101	0.101
10 "	0.124	0.140	0.114	0.085
15 "	0.149	0.161	0.122	0.089
20 "	0.173	0.185	0.131	0.100
25 "	0.194	0.185	0.124	0.101
30 "	0.194	0.187	0.115	0.109
35 "	0.192	0.183	0.115	0.112
40 "	0.183	0.140	0.121	0.096
45 "	0.164	0.154	0.117	0.098
50 "	0.142	0.135	0.110	0.101
55 "	0.138	0.122	0.114	0.128
60 "	0.144	0.119	0.124	0.136
65 "	0.133	0.128	0.124	0.135
70 "	0.142	0.131	0.122	0.129
75 "	0.131	0.146	0.122	0.126
80 "	0.116	0.151	0.100	0.131
85 "	0.119	0.135	0.094	0.135
90 "	0.107	0.131	0.089	0.140
100 "	0.091	0.142	0.089	0.136
110 "	0.091	0.093	0.092	0.144
120 "	0.100	0.087	0.101	0.122
130 "	0.089	0.098	0.101	0.085
140 "	0.076	0.096	0.119	0.080
150 "	0.084	0.076	0.101	0.092

Group III.

No 5 (male)				No. 6 (male)	
Date	Jan. 11, 30	Jan. 16. 30	Jan. 20, 30	Oct. 15. 30	Oct. 18, 30
Age	3 y. 6 m.			3 y. 10 m.	
Weight	14.900 kg.	14.500 kg.	14.500 kg.	15.100 kg.	15.300 kg.
Diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14½ hours	14½ hours	14½ hours	14½ hours	14½ hours
Glucose per kg. of b. w.	2 gm.	2 gm.	1 gm.	1.5 gm.	1.5 gm.
Time for ingestion	5 min.	5 min.	3 min.	1½ min.	1½ min.
Fasting bl. s. $\frac{1}{10}$	0.089	0.083	0.079	0.097	0.095
0 Min.	0.088	0.078	0.084	0.092	0.090
5 »	0.120	0.112	0.107	0.086	0.097
10 »	0.141		0.121	0.104	0.112
15 »	0.152	0.151	0.138	0.124	0.123
20 »	0.188	0.172	0.142	0.136	0.130
25 »	0.188	0.179	0.151	0.137	0.137
30 »	0.192	0.181	0.155	0.137	0.128
35 »	0.192	0.170	0.146	0.152	0.125
40 »	0.181	0.165	0.128	0.138	0.125
45 »		0.154	0.131	0.138	0.134
50 »	0.176	0.158	0.131	0.136	0.130
55 »	0.183	0.151	0.147	0.120	0.130
60 »		0.152	0.140	0.113	0.121
65 »	0.172	0.149	0.140	0.099	0.121
70 »	0.163	0.134	0.138	0.101	0.111
75 »	0.163	0.142	0.130	0.097	0.102
80 »	0.141	0.133	0.126	0.088	0.091
85 »	0.138	0.131	0.111	0.103	0.094
90 »	0.141	0.133	0.091	0.092	0.094
100 »	0.127	0.129	0.058	0.099	0.094
110 »	0.090	0.112	0.053	0.081	0.098
120 »	0.088	0.112	0.051	0.083	0.091
130 »	0.090	0.090	0.066	0.081	0.091
140 »	0.087	0.080	0.069	0.068	0.068
150 »			0.066	0.072	0.066

Group III.

No. 7 (male)			No. 8 (female)		No. 9 (female)	
Date	Jan. 13, 30	Jan. 18, 30	Sep. 26, 30	Sep. 30, 30	Oct. 21, 30	Oct. 24, 30
Age	3 y. 8 m.		4 y. 4 m.		5 y. 1 m.	
Weight	14.700 kg.	14.700	17.900 kg.	18.000 kg.	19.600	19.800 kg.
Diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14½ hours	14½ hours	15 hours	15 hours	14½ hours	14½ hours
Glucose per kg. of b. w.	2 gm.	2 gm.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.
Time for ingestion	5 min.	6 min.	4 min.	3 min.	2 min.	2 min.
Fasting bl. s. $\frac{6}{10}$	0.079	0.089	0.098	0.097	0.090	0.081
0 Min.	0.079	0.101	0.098		0.089	0.081
5 "	0.097	0.112	0.126	0.107	0.120	0.110
10 "	0.103	0.131	0.119	0.124	0.140	0.133
15 "	0.115	0.149		0.140	0.152	0.145
20 "	0.125	0.153	0.142	0.146	0.161	0.140
25 "	0.140	0.154	0.147	0.155	0.163	0.151
30 "	0.136	0.153	0.154	0.158	0.167	0.163
35 "	0.138	0.154	0.154	0.164	0.160	0.165
40 "	0.152	0.156	0.138	0.158	0.163	0.161
45 "	0.152	0.156	0.143	0.144	0.152	0.154
50 "	0.152	0.154	0.136	0.130	0.160	0.145
55 "	0.140	0.158	0.136	0.139	0.160	0.142
60 "	0.145	0.162	0.115	0.109	0.160	0.110
65 "	0.140	0.153		0.105	0.158	0.105
70 "	0.136	0.140	0.122	0.100	0.142	0.096
75 "	0.134	0.124		0.100	0.117	0.094
80 "	0.124	0.117	0.108	0.100	0.112	0.096
85 "	0.124	0.105		0.102	0.103	0.107
90 "	0.120	0.104	0.090	0.114	0.096	0.107
100 "	0.101	0.106	0.105	0.114	0.083	0.119
110 "	0.101	0.094	0.126	0.117	0.096	0.096
120 "	0.103	0.105	0.112	0.102	0.103	0.090
130 "	0.096	0.096	0.103	0.089	0.092	0.094
140 "	0.088	0.105	0.105	0.093	0.090	0.101
150 "	0.092	0.107	0.101	0.093	0.080	0.087

Group III.

No. 10 (female)			No. 11 (male)	No. 12 (male)	
Date	Oct. 22, 30	Oct. 25, 30	Oct. 18, 30	Nov. 27, 30	Dec. 1, 30
Age	5 y. 7 m.		5 y. 8 m.	6 y. 3 m.	
Weight	20.800 kg.	21.000 kg.	18.500 kg.	20.100 kg.	20.100 kg.
Diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14½ hours	14½ hours	14½ hours	14½ hours	14½ hours
Glucose per kg. of b. w.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.
Time for ingestion	1 min.	1 min.	1 min.	2 min.	2 min.
Fasting bl. s. %	0.083	0.088	0.090	0.086	0.076
0 Min.	0.085	0.093	0.086	0.085	0.081
5 »	0.089	0.097		0.109	0.108
10 »	0.098	0.113	0.105	0.128	0.127
15 »	0.120	0.132		0.140	0.149
20 »	0.138	0.143	0.111	0.144	0.145
25 »	0.138	0.136		0.158	0.145
30 »	0.138	0.116	0.117	0.176	0.145
35 »	0.142	0.115		0.176	0.151
40 »	0.147	0.111	0.122	0.167	0.147
45 »	0.147	0.108		0.164	0.143
50 »	0.152	0.104	0.120	0.153	0.134
55 »	0.149	0.102		0.171	0.136
60 »	0.134	0.111	0.122	0.169	0.127
65 »	0.122	0.111		0.156	0.127
70 »	0.119	0.110		0.133	0.117
75 »	0.117	0.106	0.104	0.135	0.105
80 »	0.120	0.106		0.131	0.108
85 »	0.112	0.110		0.130	0.103
90 »	0.098	0.090	0.098	0.133	0.103
100 »	0.098	0.088		0.109	0.099
		105 Min.	0.086		
110 »	0.110	0.102		0.109	0.090
120 »	0.107	0.118	0.081	0.121	0.089
130 »	0.081	0.108		0.116	0.074
		135 »	0.075		
140 »	0.063	0.084		0.107	0.056
150 »	0.051	0.090	0.076	0.105	0.044

Group III.

No. 13 (female)			No. 14 (male)		No. 15 (female)	
Date	Nov. 13, 30	Nov. 15, 30	Oct. 29, 30	Nov. 1, 30	Oct. 14, 30	Oct. 17, 30
Age	7 y. 2 m.		7 y. 6 m.		7 y. 11 m.	
Weight	19.000 kg.	19.200 kg.	22.200 kg.	22.200 kg.	22.500 kg.	22.500 kg.
Diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14½ hours	14½ hours	14½ hours	14½ hours	14½ hours	14½ hours
Glucose per kg. of b. w.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.
Time for ingestion	1 min.	2 min.	2 min.	4 min.	3 min.	2 min.
Fasting bl. s. $\frac{g}{100}$	0.095	0.094	0.095	0.083	0.089	0.084
0 Min.	0.092	0.094	0.095	0.083	0.089	0.084
5 »	0.110	0.103	0.115	0.099	0.099	0.113
10 »	0.117		0.125	0.127	0.098	0.128
15 »	0.133	0.127	0.139	0.120	0.119	0.137
20 »	0.151	0.152	0.138	0.110	0.126	0.152
25 »	0.152	0.148	0.163	0.101	0.140	0.153
30 »	0.147	0.148	0.165	0.103	0.142	0.155
35 »	0.140	0.129	0.157	0.108	0.152	0.150
40 »	0.131	0.115	0.157	0.115	0.142	0.141
45 »	0.131	0.103	0.152	0.120	0.147	0.121
50 »	0.117	0.097	0.147	0.129	0.145	0.121
55 »	0.112	0.099	0.134	0.131	0.140	0.116
60 »	0.099	0.097	0.132	0.125	0.129	0.106
65 »	0.090	0.097	0.132	0.124	0.124	0.106
70 »	0.074		0.122	0.122	0.108	0.104
75 »	0.078	0.097	0.112	0.118	0.103	0.104
80 »	0.085	0.101	0.103	0.118	0.096	0.108
85 »	0.074	0.088		0.111	0.092	0.111
90 »	0.071	0.095	0.099	0.105	0.089	0.095
100 »	0.089	0.112	0.092	0.106	0.074	0.088
110 »	0.103	0.122	0.094	0.094	0.074	0.088
120 »	0.105	0.106	0.086	0.085	0.074	0.084
130 »	0.108	0.092	0.086	0.088	0.083	0.091
140 »	0.096	0.076	0.088	0.087	0.089	0.090
150 »	0.096	0.085	0.088	0.076	0.105	0.084

Group III.

No. 16 (female)			No. 17 (female)		No. 18 (male)	
Date	Nov. 26, 30	Nov. 29, 30	Oct. 27, 30	Oct. 30, 30	July 26, 30	Aug. 2, 30
Age	8 y. 9 m.		9 y. 7 m.		10 y.	
Weight	22.500 kg.	22.700 kg.	33.800 kg.	34.000 kg.	22.100 kg.	22.100 kg.
Diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14½ hours	14½ hours	14½ hours	14½ hours	14½ hours	14½ hours
Glucose per. kg. of b. w.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.
Time for ingestion	3 min.	2 min.	2 min.	2½ min.	5 min.	5 min.
Fasting bl. s. %	0.092	0.082	0.096	0.099	0.092	0.086
0 Min.	0.097	0.087	0.090	0.098	0.098	0.100
5 »	0.105	0.103	0.124	0.115	0.100	0.112
10 »	0.111	0.126	0.139	0.135	0.121	0.151
15 »	0.120	0.142	0.150	0.147	0.126	0.162
20 »	0.147	0.154	0.175	0.151	0.151	0.180
25 »	0.147	0.158	0.166	0.160	0.155	0.192
30 »	0.147	0.156	0.184	0.165	0.187	0.198
35 »	0.143	0.142	0.179	0.147	0.184	0.201
40 »	0.143	0.145	0.175	0.156	0.194	0.201
45 »	0.125	0.145	0.172	0.154	0.185	0.183
50 »	0.132	0.128	0.174	0.162	0.187	0.176
55 »	0.127	0.121		0.160	0.182	0.183
60 »		0.122	0.166	0.163	0.185	0.160
65 »	0.113	0.119	0.168	0.166		
70 »	0.103		0.163	0.156	0.180	0.169
75 »	0.111		0.161	0.147		
80 »	0.099	0.089	0.157	0.138	0.157	0.114
85 »	0.099	0.089	0.152	0.144		
90 »	0.103	0.092	0.143	0.128	0.149	0.126
100 »	0.106	0.101	0.124	0.110	0.110	0.142
110 »	0.111	0.101	0.112	0.096	0.104	0.124
120 »	0.106	0.098	0.104	0.080	0.104	0.116
130 »	0.111	0.087	0.097	0.073	0.119	0.098
140 »	0.110	0.091	0.094	0.071	0.109	0.098
150 »	0.099	0.087	0.079	0.091	0.093	0.087

Group III.

No. 19 (female)			No. 20 (male)		No. 21 (male)	
Date	Oct. 2, 30	Oct. 6, 30	Nov. 6, 30	Nov. 8, 30	Nov. 5, 30	Nov. 7, 30
Age	12 y. 2 m.		12 y. 3 m.		13 y. 1 m.	
Weight	29.200	29.600 kg.	33.200 kg.	34.000 kg.	32.100 kg.	32.100 kg.
Diet	Ord. diet	Ord. diet.	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14½ hours	14½ hours	15 hours	15 hours	14 hours	14 hours
Glucose per kg. of b. w.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.	1.5 gm.
Time for ingestion	3 min.	2 min.	2 min.	2 min.	2 min.	2 min.
Fasting bl. s. %	0.091	0.094	0.094	0.086	0.094	0.088
0 Min.	0.097	0.092	0.094	0.089	0.098	0.088
5 »	0.091	0.085	0.101	0.096	0.098	0.102
10 »	0.093	0.100	0.119	0.110	—	0.116
15 »	0.097	0.114	0.136	0.117	0.116	0.130
20 »	0.114	0.119	0.143	0.124	0.132	0.146
25 »	0.114	0.135	0.151	0.131	0.151	0.153
30 »	0.119	0.129	0.151	0.129	0.160	0.153
35 »	0.126	0.136	0.158	0.138	0.158	0.151
40 »	0.123	0.136	0.160	0.135	0.155	0.150
45 »	0.128	0.144	0.151	0.122	0.144	0.146
50 »	0.142	0.135	0.138	0.117	0.142	0.144
55 »	0.139	0.142	0.136	0.107	0.142	0.137
60 »	0.148	0.147	0.129	0.109	0.135	0.133
65 »	0.141	0.147	0.127	0.122	0.128	0.135
70 »	—	0.142	0.119	0.112	0.126	0.114
75 »	0.146	0.136	0.117	0.109	0.118	0.118
80 »	0.118	0.138	0.108	0.105	0.109	0.109
85 »	0.130	0.140	0.119	0.101	0.104	0.107
90 »	0.114	0.136	0.122	0.098	0.100	0.104
100 »	—	0.138	0.126	0.115	0.107	0.098
110 »	0.116	0.133	0.120	0.112	0.114	0.106
120 »	0.111	0.133	0.110	0.101	0.105	0.112
130 »	0.116	0.122	0.099	0.094	0.114	0.111
140 »	0.118	0.122	0.099	0.096	0.109	0.088
150 »	0.121	0.119	0.115	0.096	0.105	0.080

Group III.

No. 22 (female)		
Date	Nov. 18, 1930	Nov. 21, 1930
Age	13 y. 8 m.	
Weight	42.600 kg.	42.600 kg.
Diet	Ord. diet	Ord. diet
Fasting period	14½ hours	14½ hours
Glucose per kg of b. w.	1.5 gm.	1.5 gm.
Time for ingestion	3 min.	3 min.
Fasting bl. s. σ_0	0.093	0.084
0 Min.	0.084	0.096
5 »	0.087	0.099
10 »	0.100	0.103
15 »	0.110	0.113
20 »	0.116	0.117
25 »	0.119	0.117
30 »	0.119	0.118
35 »	0.123	0.124
40 »	0.123	0.124
45 »	0.114	0.120
50 »	0.117	0.120
55 »	0.119	0.125
60 »	0.112	0.125
65 »	0.121	0.125
70 »	0.114	0.118
75 »	0.114	0.118
80 »	0.110	0.124
85 »	0.107	0.120
90 »	0.112	0.118
100 »	0.109	0.115
110 »	0.110	0.118
120 »	0.105	0.111
130 »	0.105	0.110
140 »	0.098	0.115
150 »	0.100	0.108

Glucose — Saccharose.

No. 1 (male)				No. 2 (male)		
Date	May 10, 1928	May 19, 28	May 21, 28	Apr. 19, 28	Apr. 24, 28	
Age	1 m. 21 d.	1 m. 30 d.	2 m. 1 d.	2 m. 8 d.	2 m. 13 d.	
Weight	4.500 kg.	4.630 Kg.	4.630 kg.	4.000 kg.	4.150 kg.	
Diet	1 M + 1 B 125 cc. × 7	1 M + 1 B 150 cc. × 7	Same diet	1 M + 1 B 125 cc. × 7	Same diet	
Fasting period	6 hours	6 hours	6 hours	6 hours	6 hours	
Dose per kg. of b. w.	1 gm. gluc.	2 gm. gluc.	2 gm. sacch.	2 gm. gluc.	2 gm. sacch.	
Time for ingestion	5 min.	4 min.	4 min.	7 min.	8 min.	
Fasting bl. s. %	0.087	0.071	0.081	0.076	0.089	
0 Min.	0.089	0.074	0.099	0 Min.	0.075	0.082
5 »	0.128	0.100	0.121	2 »	—	—
10 »	0.105	—	0.139	10 »	0.105	0.114
15 »	0.115	0.114	0.155	12 »	0.114	0.121
20 »	0.151	0.143	0.171	20 »	0.127	0.129
25 »	0.128	0.163	0.175	22 »	0.128	0.121
30 »	0.138	0.174	0.182	30 »	0.146	0.117
35 »	0.119	0.180	0.182	32 »	0.145	0.131
40 »	—	0.182	0.186	40 »	0.145	0.107
45 »	0.124	0.187	0.186	42 »	0.141	—
50 »	0.103	0.191	0.186	50 »	0.132	0.110
55 »	0.102	0.206	0.195	52 »	0.127	0.105
60 »	0.096	0.198	0.201	60 »	0.127	0.096
65 »	0.107	0.208	—	62 »	—	0.096
70 »	0.087	0.195	0.199	70 »	0.111	0.083
75 »	—	0.180	0.197	72 »	—	0.083
80 »	0.090	0.173	—	80 »	0.104	0.078
85 »	—	0.157	0.175	82 »	0.102	0.076
90 »	0.084	0.137	0.179	90 »	0.077	0.076
100 »	—	0.133	0.141	92 »	0.079	0.076
110 »	0.094	0.110	0.116	100 »	0.098	0.074
120 »	0.101	0.095	0.111	102 »	0.090	—
130 »	—	0.068	0.072	110 »	0.081	0.083
135 »	0.096	—	—	112 »	0.083	—
140 »	—	0.056	0.073	120 »	0.072	0.082
150 »	0.075	0.055	0.070	122 »	0.072	0.080
				135 »	0.065	0.082
				137 »	0.063	0.082
				150 »	0.056	0.082
				152 »	0.059	0.078

Glucose — Saccharose.

No. 3 (male)			No. 4 (male)	
Date	May 5, 1928	May 12, 1928	May 18, 1928	June 6, 1928
Age	2 m. 20 d.	2 m. 27 d.	6 m. 6 d.	6 m. 25 d.
Weight	3.350 kg.	3.500 kg.	7.600 kg.	7.200 kg.
Diet	1 M + 1 B 125 cc. × 7	Same diet	G 225 gm. × 2 3 M + 1 B 225 cc. × 3	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours
Dose per kg. of b. w.	2 gm. gluc.	2 gm. sacch.	2 gm. gluc.	2 gm. sacch.
Time for ingestion	14 min.	10 min.	4 min.	3 min.
Fasting bl. s. %	0.087	0.087	0.070	0.073
0 Min.	0.074	0.078	0.079	0.081
5 »	0.121	0.112	0.094	0.081
10 »	0.143	0.133	0.109	0.096
15 »	0.172	0.160	0.116	0.117
20 »	0.164	0.183	0.135	0.125
25 »	0.204	0.194	0.148	0.136
30 »	0.222	—	—	0.149
35 »	0.237	0.194	0.112	0.141
40 »	0.260	0.192	0.121	0.159
45 »	0.242	0.178	0.116	0.154
50 »	0.242	0.178	0.116	0.158
55 »	0.239	0.178	0.110	0.162
60 »	0.208	0.180	0.110	0.159
65 »	—	—	—	0.161
70 »	0.185	0.167	0.117	0.132
75 »	—	—	0.105	0.057
80 »	0.163	0.149	0.096	0.068
85 »	—	0.133	0.100	0.121
90 »	0.134	0.127	0.098	0.116
95 »	—	0.112	0.075	0.125
100 »	0.107	0.108	0.055	0.084
105 »	—	0.100	0.055	0.077
110 »	0.090	0.082	0.059	0.068
115 »	—	0.083	0.069	0.064
120 »	0.077	0.069	0.071	0.055
130 »	0.076	0.082	0.080	0.065
140 »	0.074	0.078	0.084	—
150 »	0.076	0.073	0.087	—

Glucose — Saccharose.

No. 5 (male)				No. 6 (male)		
Date	April 12, 28	May 15, 28	Jun 29, 28	Apr. 20, 28	May 3, 28	
Age	6 m. 16 d.	7 m. 19 d.	9 m. 3 d.	8 m. 11 d.	8 m. 14 d.	
Weight	7.190 kg.	8.000 kg.	8.450 kg.	8.220 kg.	8.300 kg.	
Diet	M 225 cc. × 2 G 225 gm. × 2 Omg. 225 gm. × 1	Same diet	Same diet	M 225 cc. × 2 G 225 gm. × 2 Omg. 225 gm. × 1	Same diet	
Fasting period	6 hours	6½ hours	6½ hours	6½ hours	6 hours	
Dose per kg. of b. w.	1 gm. gluc.	2gm. sacch.	2 gm. gluc	2 gm. gluc.	2gm. sacch.	
Time for ingestion	10 min.	10 min.	13 min.	15 min.	17 min.	
Fasting bl. s. %	0.062	0.070	0.085	0.084	0.083	
0 Min.	0.075	0.073	0.096	0 Min.	0.146	0.107
5 »	—	0.076	0.122	5 »	0.170	0.132
10 »	0.070	0.087	0.154	10 »	0.204	0.146
15 »	—	0.098	0.163	15 »	0.186	0.146
20 »	0.093	0.112	0.167	20 »	0.188	0.135
25 »	—	0.142	0.181	25 »	0.197	0.135
30 »	0.099	0.135	0.185	30 »	0.182	0.116
35 »	—	0.126	0.189	35 »	0.182	—
40 »	0.104	0.127	0.185	40 »	0.177	0.116
45 »	—	0.120	0.189	45 »	0.166	0.107
50 »	0.096	0.140	0.176	50 »	0.175	0.102
55 »	—	0.131	0.165	55 »	0.186	—
60 »	0.089	0.137	0.169	60 »	0.182	0.104
65 »	—	0.137	0.174	70 »	—	0.105
70 »	0.099	0.128	0.156	80 »	0.131	0.086
75 »	—	0.140	0.136	90 »	0.132	0.075
80 »	0.110	0.123	0.120	100 »	0.142	0.064
85 »	—	0.123	0.122	110 »	0.121	0.070
90 »	0.101	0.126	0.120	120 »	0.098	0.084
95 »	—	0.126	0.122	135 »	0.072	0.095
100 »	0.101	0.123	—	150 »	0.082	0.087
105 »	—	0.121	0.110			
110 »	0.079	0.104	0.072			
115 »	—	0.082	0.062			
120 »	0.075	0.082	0.051			
130 »	—	—	0.045			
135 »	0.082	0.065	0.063			
140 »	—	0.063	0.060			
150 »	0.077	0.064	0.067			

Coeliac Disease.

No. 1 (male)				
Date	June 13, 1930	June 17, 1930	June 26, 1930	June 28, 1930
Age	1 y. 11 m.			
Weight	7.850 kg.	8.000 kg.	8.250 kg.	8.250 kg.
Diet	Milk, gruel, oatmeal gr., rice meal gr., crackers, lemonade	Same diet	Same diet	Ord. diet
Fasting period	14 hours	14 hours	14 hours	14 hours
Glucose per kg. of b. w.	2 gm.	2 gm.		4 gm.
Adrenalin 0/100 sol.			0.3 cc. subc.	
Time for ingestion	2 min.	2 min.		6 min.
Fasting bl. s. $\frac{0}{100}$	0.084	0.092	0.083	0.085
0 Min.	0.085	0.092	0.085	0.087
5 »	0.091	0.090	0.092	0.089
10 »	0.084	0.083	0.095	0.083
15 »	0.084	0.094	0.108	0.082
20 »	0.087	0.094	0.106	0.092
25 »	0.084	0.087	0.111	0.087
30 »	0.085	0.090	0.116	0.089
35 »	0.093	0.088	0.111	0.100
40 »	0.085	0.088	0.108	0.089
45 »	0.082	0.096	0.115	0.092
50 »	0.085	0.087	0.108	0.089
55 »	0.091	0.092	0.143	0.096
60 »	0.084	0.097	0.116	0.085
65 »	—	—	—	—
70 »	0.084	0.085	0.113	0.087
75 »	—	—	—	—
80 »	0.071	0.088	0.109	0.076
85 »	—	—	—	—
90 »	0.080	0.092	0.106	0.076
100 »	0.084	0.088	0.104	0.076
110 »	0.082	0.087	0.101	0.073
120 »	0.080	0.094	0.088	0.076
130 »	0.084	0.083	0.083	0.083
140 »	0.080	0.088	0.088	0.080
150 »	0.078	0.090	0.081	0.083

Celiac Disease.

No. 1 (male)		No. 2 (female)		
Date	June 29, 1930	July 24, 1929	July 27, 1929	July 31, 1929
Age	1 y. 11 m.	2 y. 7 m.		
Weight	8.250 kg.	9.3000 kg.	9.450 kg.	9.550 kg.
Diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14 hours	14 hours	14 hours	14 hours
Glucose per kg of b. w.	2 gm.	2 gm.	2 gm.	20% sol. 6 gm.
Adrenalin 0.00 sol.	0.3 cc. subc.			
Time for ingestion	2 min.	3 min.	2 min.	3 min.
Fasting bl. s. %	0.091	0.087	0.070	0.087
0 Min.	0.087	0.097	0.081	0.091
5 »	0.097	—	—	—
10 »	0.092	0.090	0.081	0.117
15 »	0.079	—	—	—
20 »	0.087	0.090	0.083	0.116
25 »	0.108	—	—	—
30 »	0.111	0.090	0.085	0.121
35 »	0.129	—	—	—
40 »	0.122	0.086	0.080	0.137
45 »	0.132	—	—	—
50 »	0.141	0.092	0.081	0.148
55 »	0.147	—	—	—
60 »	0.140	0.090	0.080	0.164
65 »	—	—	—	—
70 »	0.141	0.090	0.096	0.148
75 »	—	—	—	—
80 »	0.138	0.093	0.092	0.148
85 »	—	—	—	—
90 »	0.136	0.095	0.092	0.137
100 »	0.138	—	0.092	0.141
110 »	0.131	0.095	0.085	0.137
120 »	0.125	0.097	0.081	0.130
130 »	0.111	0.107	0.074	0.124
140 »	0.113	0.095	0.090	0.119
150 »	0.101	0.097	—	0.112

*Coeliac Disease.***No. 2 (female)**

Date	Dec. 16, 1929	March 1, 1930	March 5, 1930	March 7, 1930
Age	2 y. 11 m.	3 y. 1 m.		
Weight	9.850 kg.	10.100 kg.	10.150 kg.	10.150 kg.
Diet	Ord. diet + milk	Casein-barley gruel, fruit soups, oatmeal gruel, bananas and other fruit, crackers, zwiebacks.		Same diet
Fasting period	14 hours	14 hours	14 hours	14 hours
Glucose per kg. of b. w.	2 gm.	2 gm.		2 gm. +
Adrenalin 6/100 sol.			0.4 cc. subc.	0.4 cc subc.
Time for ingestion	3 min.	3 min.		3 min.
Fasting bl. s. %	0.081	0.095	0.096	0.070
0 Min.	0.080	0.095	0.096	0.082
5 »	—	—	0.097	0.093
10 »	0.087	0.102	0.101	0.103
15 »	—	—	0.110	0.121
20 »	0.087	0.105	0.120	0.130
25 »	—	—	0.138	0.139
30 »	0.084	0.107	0.136	0.158
35 »	—	—	0.149	0.158
40 »	0.080	0.095	0.152	0.171
45 »	—	—	0.161	0.175
50 »	0.086	0.084	0.170	0.189
55 »	—	—	0.163	0.191
60 »	0.087	0.091	0.161	0.200
65 »	—	—	0.143	0.197
70 »	0.089	0.096	0.140	0.217
75 »	—	—	0.150	0.204
80 »	0.087	0.104	0.138	0.200
85 »	—	—	0.127	0.176
90 »	0.089	0.107	0.127	0.171
100 »	0.086	0.105	0.108	0.157
110 »	0.084	0.096	0.101	0.108
120 »	0.077	0.098	0.092	—
130 »	0.069	0.102	0.096	0.091
140 »	0.086	0.096	0.099	0.088
150 »	0.077	0.093	0.096	0.069

*Celiac Disease.***No. 2 (female)**

Date	Apr. 1, 1931	Apr. 8, 1931	Apr. 15, 1931
Age	4 y. 3 m.		
Weight	12.909 kg.	13.150 kg.	13.150 kg.
Diet	Ord. diet + milk	Same diet	Same diet
Fasting period	14 hours	14 $\frac{1}{2}$ hours	14 hours
Glucose per. kg. of b. w.	2 gm.	2 gm.	6 gm.
Time for ingestion	4 min.	3 min.	12 min.
Fasting bl. s. σ_0	0.094	0.087	0.095
0 Min.	0.099	0.087	0.102
10 »	0.099	0.089	0.107
20 »	0.094	0.087	0.118
30 »	0.101	0.093	0.128
40 »	0.120	0.105	0.134
50 »	0.105	0.099	0.141
60 »	0.107	0.097	0.134
70 »	0.099	0.112	0.130
80 »	0.090	0.102	0.118
90 »	0.090	0.087	0.114
100 »	0.094	0.084	0.109
110 »	0.096	0.096	0.109
120 »	0.089	0.095	0.101
130 »	0.096	0.104	0.104
140 »	0.099	0.095	0.104
150 »	0.099	0.098	0.109

Coeliac Disease.

No. 3 (male)				
Date	Sept. 21, 1928	Oct. 3, 1928	Nov. 11, 1928	Nov. 26, 1928
Age	3 y. 10 m.		3 y. 11 m.	
Weight	11.300 kg.	11.500 kg.	12.000 kg.	12.400 kg.
Diet	Ord. diet ÷ milk	Same diet	Casein-barley gruel, fruit soups oatmeal gruel, bananas and other fruit, crackers, vegetable purees, scraped broiled meat zwiebacks.	
Fasting period	14 hours	14 hours	14 hours	14 hours
Glucose per kg. of b. w.	1.5 gm.	1.5 gm.	1.5 gm.	2 gm.
Time for ingestion	2 min.	1 min.	1 min.	2 min.
Fasting bl. s. %	0.071	0.071	0.070	0.077
0 Min.	0.069	0.078	0.069	0.076
5 »	—	—	—	—
10 »	0.093	0.075	0.082	0.082
15 »	—	—	—	—
20 »	0.093	0.080	0.090	0.092
25 »	—	—	—	—
30 »	0.096	0.078	0.088	0.093
40 »	0.100	0.078	0.089	0.097
50 »	0.099	0.080	0.090	0.093
60 »	0.098	0.084	0.087	0.103
75 »	0.090	0.075	0.073	0.110
90 »	0.090	0.087	0.081	0.095
105 »	0.092	0.078	0.087	0.088
120 »	0.082	0.075	0.078	0.071
135 »	0.081	0.073	0.068	0.067
150 »	0.069	0.078	0.073	0.087
180 »	0.063	0.080	—	0.070

Celiac Disease.

No. 3 (male)				
Date	Dec. 6, 1928	Nov. 5, 1928	Sep. 28, 1928	Oct. 19, 1928
Age	4 years	3 y. 11 m.	3 y. 10 m.	3 y. 10½ m.
Weight	12.500 kg.	11.300 kg.	11.350 kg.	11.800 kg.
Diet	Casein-barley gruel, fruit soups, oatmeal gruel, bananas and other fruit, crackers, vegetable purees, scraped broiled meat zwiebacks.		Ord. diet ÷ milk	Casein-barley gruel, bananas
Fasting period	14 hours	14 hours	14 hours	14 hours
Glucose per kg. of b. w.	15% sol.	Levulose 1.5 gm.	1.5 gm.	
Adrenalin % sol.	4 gm.		0.4 cc. subc.	0.4 cc. subc.
Time for ingestion	2 min.	2 min.	2 min.	
Fasting bl. s. %	0.070	0.071	0.078	0.077
0 Min.	0.084	0.065	0.077	0.072
5 »	—	—	0.091	0.072
10 »	—	0.068	0.116	0.090
15 »	0.136	—	0.124	0.105
20 »	—	0.084	0.146	0.127
25 »	—	—	0.158	—
30 »	0.147	0.090	0.180	0.141
35 »	—	—	—	—
40 »	—	0.092	0.194	0.142
45 »	0.127	—	—	—
50 »	—	0.085	0.206	0.126
55 »	—	—	—	—
60 »	0.119	0.082	0.213	0.114
65 »	—	—	—	—
70 »	—	0.080	0.202	—
75 »	0.094	—	—	0.092
80 »	—	0.083	0.211	—
85 »	—	—	—	—
90 »	0.098	0.088	0.221	—
105 »	0.098	0.084	0.221	0.083
120 »	0.087	0.085	0.201	0.075
135 »	—	0.083	0.188	0.078
150 »	0.060	0.081	0.173	0.083
180 »	0.084	0.080	0.127	0.073
210 »	0.079		0.078	0.079
240 »	0.091		0.081	—

Celiac Disease.

No. 3 (male)				No. 4 (female)	
Date	May 16, 30	May 20, 30	May 23, 30	Sep. 13, 30	Sep. 16, 30
Age	5 y. 6 m.			5 y. 7 m.	
Weight	12.200 kg.	12.400 kg.	12.700 kg.	17.100 kg.	17.400 kg.
Diet	Oatmeal gruel buttermilk, fruit, mashed potatoes, fruit soup, zwiebacks, wheat bread.			Oatmeal gruel, casein-barley gruel, bananas, crackers, wheat bread with little butter, meat balls.	
Fasting period	15 hours	14 hours	14 hours	14 hours	14 hours
Glucose per kg. of b. w. Adrenalin $\frac{0}{100}$ sol.	2 gm.	2 gm.	0.4 cc. subc.	1.5 gm.	1.5 gm.
Time for ingestion	3 min.	4 min.		2 min.	2 min.
Fasting bl. s. $\frac{0}{100}$	0.079	0.095	0.088	0.084	0.085
0 Min.	0.079	0.102	0.077	0.082	0.084
5 "	—	—	—	0.087	0.089
10 "	0.088	0.128	0.109	0.087	0.100
15 "	—	—	—	0.084	0.091
20 "	0.111	0.137	0.126	0.086	0.105
25 "	—	—	—	0.084	0.094
30 "	0.106	0.137	0.139	0.086	0.100
35 "	—	—	—	—	—
40 "	0.116	0.132	0.139	0.091	0.100
45 "	—	—	—	0.100	0.093
50 "	0.102	0.126	0.146	0.096	0.103
55 "	—	—	—	0.102	0.105
60 "	0.090	0.103	0.150	0.102	0.108
65 "	—	—	—	0.095	—
70 "	0.087	0.096	0.139	0.095	0.102
75 "	—	—	—	—	—
80 "	0.074	—	0.126	0.089	0.103
85 "	—	—	—	—	—
90 "	0.069	—	0.117	0.087	0.094
100 "	0.083	—	0.100	0.100	0.103
110 "	0.083	—	0.093	0.087	0.102
120 "	0.094	0.093	0.093	0.087	0.100
130 "	0.109	0.086	—	0.096	—
135 "	—	—	0.086	—	—
140 "	0.104	0.086	—	0.089	0.100
150 "	0.099	0.091	0.068	0.098	0.091

Celiac Disease.

No. 4 (female)				No. 5 (female)	
Date	Sep. 23, 30	Oct. 7, 30	Oct. 9, 30	Feb. 22, 28	Feb. 26, 28
Age	5 y. 7 m.			10 y. 9 m.	
Weight	17.200 kg.	16.500 kg.	17.100	22.000 kg.	22.000 kg.
Diet	Ord. diet + milk . Casein-barley gruel, fruit, lemonade.		Same diet	Ord. diet + milk . Fruit and vegetables	Same diet
Fasting period	14 hours	14 hours	14 hours	14 hours	14 hours
Glucose per kg. of b. w. Adrenalin $\frac{1}{100}$ sol.	4 gm.		1.5 gm. + 0.4 cc. subc.	1 gm.	1 gm.
Time for ingestion	5 min.		3 min.	2 min.	3 min.
Fasting bl. s. $\frac{1}{100}$	0.092	0.076	0.078	0.070	0.097
0 Min.	—	0.090	0.082	0.079	0.098
5 "	0.096	0.086	0.096	—	—
10 "	0.092	0.103	0.111	0.073	0.104
15 "	0.085	0.115	0.131	—	—
20 "	0.092	0.132	0.149	0.081	0.109
25 "	0.092	0.150	0.176	—	—
30 "	0.089	0.154	0.185	0.082	0.108
35 "	0.096	0.179	0.196	—	—
40 "	0.090	0.186	0.205	0.083	0.106
45 "	0.089	0.184	0.209	—	—
50 "	0.094	0.184	0.211	0.083	0.106
55 "	0.087	0.175	0.216	—	—
60 "	0.112	0.171	0.224	0.087	0.099
65 "		0.165	—	—	—
70 "		0.165	0.222	0.083	0.101
75 "		—	—	—	—
80 "		0.141	0.220	0.087	0.093
85 "		—	—	—	—
90 "		0.112	0.205	0.078	0.098
100 "		0.108	0.189	0.078	0.092
110 "		0.083	0.169	0.082	0.096
120 "		0.072	0.167	0.086	0.095
130 "		0.076	0.140	0.088	0.082
140 "		0.076	0.123	0.089	0.089
150 "		0.068	0.112	0.090	—

Dyspepsia.

No. 1 (female)		No. (female)	
Date	Jan. 24, 1930	May 8, 1929	May 16, 1929
Age	2 m. 2 d.	5 m. 16 d.	5 m. 24 d.
Weight	3.810 kg.	6.400 kg.	6.400 kg.
Diet	3 M + 2 B 125 cc. \times 7	3 M + 1 B 150 cc. \times 5 G 150 gm. \times 2	Same diet
Fasting period	6½ hours	6½ hours	6½ hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.
Time for ingestion	1 min.	2 min.	1 min.
Fasting bl. s. $\frac{0}{10}$	0.063	0.074	0.074
0 Min.	0.070	0.084	0.086
5 »	0.116	—	—
10 »	0.121	—	0.150
15 »	0.150	—	—
20 »	0.135	0.121	0.186
25 »	0.141	—	—
30 »	0.123	0.126	0.164
35 »	0.137	—	—
40 »	0.148	0.137	0.143
45 »	0.159	—	—
50 »	0.168	0.137	0.125
55 »	0.177	—	—
60 »	0.166	0.140	0.137
65 »	0.168	—	—
70 »	0.155	0.151	0.168
75 »	0.161	—	—
80 »	0.166	0.151	0.162
85 »	0.144	—	—
90 »	0.127	0.155	0.111
100 »	0.100	0.155	0.111
110 »	0.075	0.138	—
120 »	0.070	0.117	0.095
130 »	0.057	0.098	0.097
140 »	0.073	0.094	0.084
150 »	0.075	0.084	0.057

Dyspepsia.

No. 3 (male)			No. 4 (female)	
Date	May 12, 1930	May 17, 1930	May 15, 1930	May 22, 1930
Age	5 m. 22 d.	5 m. 27 d.	7 m. 10 d.	7 m. 17 d.
Weight	5.650 kg.	5.800 kg.	5.250 kg.	5.390 kg.
Diet	M 150 cc. \times 7 + lactic acid	Same diet	3 M + 1 B 150 cc. \times 3 gruel 150 gm. \times 2	
Fasting period	6½ hours	6½ hours	6½ hours	6½ hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	2 min.
Fasting bl. s. ‰	0.076	0.078	0.082	0.079
0 Min.	0.090	0.097	0.090	0.114
5 »	0.102	0.128	0.115	0.138
10 »	0.141	0.139	0.129	0.158
15 »	0.146	0.157	0.145	0.156
20 »	0.152	0.166	0.125	0.167
25 »	0.172	0.184	0.154	0.178
30 »	0.184	0.177	0.163	0.178
35 »	0.184	—	0.172	—
40 »	0.181	0.209	0.183	0.156
45 »	0.179	—	0.201	—
50 »	0.203	0.211	0.196	0.126
55 »	0.190	—	0.186	—
60 »	0.186	0.194	0.179	0.110
65 »	0.188	—	0.192	—
70 »	0.181	0.159	0.196	0.108
75 »	0.170	—	0.176	—
80 »	0.139	0.121	0.167	0.103
85 »	0.119	—	0.165	—
90 »	0.114	0.081	0.158	0.102
100 »	0.074	0.063	0.147	0.098
110 »	0.079	0.057	0.132	0.084
120 »	0.093	0.075	0.127	0.098
130 »	0.102	0.081	0.109	0.100
140 »	0.090	0.077	0.090	0.105
150 »	0.083	0.075	0.076	0.096

Dyspepsia.

No. 5 (male)		
Date	July 14, 1930	July 17, 1930
Age	1 y. 7 m.	
Weight	9.500 kg.	9.450 kg.
Diet	Ord. diet	Ord. diet
Fasting period	14 hours	14 hours
Glucose per kg. of b. w.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.
Fasting bl. s. %	0.078	0.092

0 Min.	0.084	0.098
5 »	0.098	0.112
10 »	0.146	0.144
15 »	0.158	—
20 »	0.178	0.140
25 »	0.193	0.147
30 »	0.189	0.153
35 »	0.185	0.155
40 »	0.160	0.155
45 »	0.157	0.173
50 »	—	0.156
55 »	0.135	0.153
60 »	0.133	0.146
65 »	—	—
70 »	0.128	0.144
75 »	—	—
80 »	0.133	0.147
85 »	—	—
90 »	0.133	0.112
100 »	0.112	0.105
110 »	0.086	0.124
120 »	0.080	0.110
130 »	0.073	0.108
140 »	0.075	0.098
150 »	—	0.087

*Cretinism.***No. 1 (female)**

Date	March 25, 1930	March 28, 30	April 26, 30	May 10, 30
Age	1 year	1 y. 3 d.	1 y. 1 m.	1 y. 44 d.
Weight	8.000 kg.	8.350 kg.	8.300 kg.	8.320 kg.
Diet	Milk, gruel, oatmeal gruel		Same diet	Same diet
Fasting period	12 hours	12 hours	12 hours	12 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	2 min.
Before Thyroid Treatment			After Thyroid Treatment	
Fasting bl. s. %	0.067	0.068	0.084	0.086
0 Min.	-0.069	0.080	0.116	0.111
5 "	—	—	0.145	0.134
10 "	0.107	0.096	0.186	0.152
15 "	—	—	0.206	0.170
20 "	0.110	0.117	0.225	0.170
25 "	—	—	0.246	0.170
30 "	0.109	0.122	0.237	0.173
35 "	—	—	0.237	0.201
40 "	0.101	0.121	0.241	0.209
45 "	—	—	0.254	0.220
50 "	0.094	0.135	0.241	0.228
55 "	—	—	0.241	0.228
60 "	0.096	0.119	0.252	0.233
65 "	—	—	—	0.228
70 "	0.091	0.110	0.244	0.233
75 "	—	—	0.244	0.209
80 "	0.089	0.105	0.233	0.186
85 "	—	—	0.222	0.166
90 "	0.083	0.087	0.193	0.157
100 "	0.078	0.084	0.143	0.118
110 "	0.064	0.084	0.123	0.098
120 "	0.074	0.071	0.099	0.102
130 "	0.071	0.064	0.092	0.090
140 "	0.073	0.062	0.081	0.090
150 "	0.067	0.058	0.084	0.081

Cretinism.

No. 2 (male)				
Date	July 4, 1930	July 7, 1930	July 19, 1930	July 23, 1930
Age	2 years			
Weight	12.850 kg.	12.500 kg.	12.200 kg.	12.200 kg.
Diet	Ord. diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	12 hours	12 hours	14 hours	14 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	3 min.	2 min.	2 min.	2 min.
Before Thyroid Treatment			After Thyroid Treatment	
Fasting bl. s. $\frac{0}{10}$	0.072	0.077	0.075	0.071
0 Min.	0.072	0.085	0.096	—
5 »	0.114	0.126	0.117	0.109
10 »	0.127	0.127	0.147	0.133
15 »	0.125	0.105	0.170	0.153
20 »	0.114	0.098	0.187	0.171
25 »	0.118	0.101	0.207	0.177
30 »	0.125	0.110	0.215	0.175
35 »	0.141	0.110	0.224	0.197
40 »	0.139	0.112	0.196	0.187
45 »	0.143	0.108	0.194	0.200
50 »	0.137	0.101	0.192	0.204
55 »	0.150	0.098	0.169	0.182
60 »	0.141	0.091	0.200	0.177
65 »	—	—	—	—
70 »	0.132	0.073	0.171	0.150
75 »	—	—	—	—
80 »	0.137	0.091	0.160	0.128
85 »	—	—	—	—
90 »	0.154	0.091	0.156	0.124
100 »	0.150	0.110	0.142	0.097
110 »	0.137	0.108	0.115	0.103
120 »	0.134	0.122	0.124	0.109
130 »	0.127	0.120	0.114	0.128
140 »	0.111	0.091	0.122	0.109
150 »	0.102	0.076	0.098	0.095

Cretinism.

No. 3 (female)		No. 4 (male)	
Date	Nov. 14, 1930	Jan. 22, 1930	Jan. 27, 1930
Age	2 y. 9 m.	4 y. 3 m.	4 y. 3 m.
Weight	11.200 kg.	14.250 kg.	14.400 kg.
Diet	Ord. diet	Ord. diet	Ord. diet
Fasting period	14 hours	14 hours	14 hours
Glucose per kg. of b. w.	1.5 gm.	2 gm.	2 gm.
Time for ingestion	1 min.	5 min.	5 min.
Fasting bl. s. $\frac{0}{100}$	0.085	0.069	0.080
0 Min.	0.092	0.068	0.094
5 "	—	0.085	0.124
10 "	0.132	0.085	0.124
15 "	—	0.094	0.113
20 "	0.124	0.097	0.129
25 "	—	0.106	0.141
30 "	0.132	0.118	0.122
35 "	—	—	0.117
40 "	0.145	0.113	0.103
45 "	—	—	0.092
50 "	0.138	0.113	0.090
55 "	—	—	—
60 "	0.136	0.110	0.088
65 "	—	—	—
70 "	0.134	0.095	0.104
75 "	—	—	—
80 "	0.115	0.076	0.099
85 "	—	—	—
90 "	0.113	0.086	0.112
100 "	0.106	0.097	0.108
110 "	0.101	0.099	0.085
120 "	0.092	0.106	0.081
130 "	0.090	0.095	0.092
140 "	0.086	—	—
150 "	0.079	0.070	0.094

Eczema.

No. 1 (male)			No.2(male)	No. 3 (male)	
Date	Sep. 5, 29	Sep. 12, 29	Feb. 21, 29	Feb. 19, 29	Feb. 22, 29
Age	3 m. 18 d.	3 m. 25 d.	5 m. 10 d.	6 m. 14 d.	6 m. 18 d.
Weight	4.130 kg.	4.200 kg.	7.500 kg.	7.450 kg.	7.450 kg.
Duration of eczema	ca. 1 month		ca. 2 month	ca. 4½ month	
Diet	3 M + 2 B 125 cc. × 7	Same diet	2 M + 1 B 175 cc. × 7	3 M + 1 B 200 cc. × 3 G 200 gr. × 2	Same diet
Fasting period	6 hours	6 hours	6½ hours	6½ hours	6½ hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	3 min.	2 min.
Fasting bl. s. $\frac{0}{10}$	0.084	0.075	0.080	0.086	0.073
0 Min.	0.082	0.079	0.080	0.119	0.089
5 »	0.112	0.118	0.115	0.142	0.109
10 »	0.134	0.138	0.136	0.162	0.131
15 »	0.171	0.143	0.145	0.174	0.142
20 »	0.168	0.154	0.158	0.182	0.153
25 »	0.171	0.179	0.169	0.196	—
30 »	0.177	0.179	0.172	0.196	0.165
35 »	—	0.201	0.183	0.209	0.178
40 »	0.182	0.197	0.169	0.211	0.185
45 »	0.182	0.172	0.169	0.200	0.192
50 »	0.206	0.166	—	0.209	0.196
55 »	0.193	0.161	0.136	—	0.189
60 »	0.199	0.150	0.120	0.216	0.174
65 »	0.191	0.150	0.112	0.203	0.153
70 »	0.179	0.139	0.115	0.207	0.110
75 »	0.155	0.122	0.120	0.194	0.110
80 »	0.152	0.111	0.133	0.198	0.089
85 »	0.144	0.108	0.133	0.191	0.085
90 »	0.126	0.109	0.140	0.165	0.085
100 »	0.125	0.101	0.136	0.165	0.089
110 »	0.097	0.101	0.115	0.151	0.089
120 »	0.093	0.118	0.076	—	0.085
130 »	0.073	0.111	0.076	—	0.082
135 »	—	—	—	0.044	—
140 »	0.061	0.108	0.074	—	0.082
150 »	0.050	0.118	0.089	0.080	—

Eczema.

No. 4. (male)				No. 5 (male)	
Date	March 4, 1930	March 8, 30	April 1, 30	Feb. 15, 30	Feb. 21, 30
Age	6 m. 4 d.	6 m. 8 d.	7 m. 1 d.	15 m. 11 d.	15 m. 17 d.
Weight	8.590 kg.	8.420 kg.	8.570 kg.	10.350 kg.	10.830 kg.
Duration of eczema	4 days	8 days	1 month	9 months.	
Diet	3 M + 1 B 200 cc. \times 5	Same diet	Same diet	3 M + 1 B 250 cc. \times 4 Mashed potatoes	Same diet
Fasting period	6½ hours	6½ hours	6½ hours	6½ hours	6½ hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	1 min.	2 min.	2 min.	2 min.	2 min.
Fasting bl. s. %	0.101	0.096	0.089	0.087	0.081
0 Min.	0.113	0.117	0.114	0.087	0.086
5 »	0.147	0.124	0.161	0.115	0.104
10 »	0.165	0.146	0.177	0.115	0.118
15 »	0.179	0.157	0.186	0.120	—
20 »	0.207	0.164	0.191	0.089	0.134
25 »	0.216	0.164	0.197	0.076	0.139
30 »	0.220	0.160	0.220	0.085	0.139
35 »	0.220	0.148	0.208	0.087	0.132
40 »	0.226	0.148	0.240	0.083	0.116
45 »	0.224	—	0.235	0.078	0.101
50 »	0.212	0.126	0.235	0.078	0.094
55 »	0.194	0.126	0.212	0.082	0.098
60 »	0.172	0.149	0.201	0.089	0.098
65 »	0.158	0.135	0.199	—	—
70 »	0.143	0.139	0.184	0.096	0.090
75 »	0.132	0.115	0.179	—	—
80 »	0.132	0.115	0.162	0.096	0.072
85 »	0.124	0.112	0.166	—	—
90 »	0.118	0.122	0.135	0.091	0.063
100 »	0.103	0.114	0.107	0.073	0.059
110 »	0.094	0.115	0.105	0.076	0.072
120 »	0.090	—	0.095	0.076	0.086
130 »	0.090	—	—	0.082	0.083
140 »	0.074	0.078	0.072	0.073	0.076
150 »	0.079	0.069	0.059	0.078	0.077

Rickets.

No. 1 (female)			No. 2 (male)		No.3(male)
Date	May 29, 29	May 31, 29	May 21, 30	May 26, 30	Sep. 10, 30
Age	6 m. 10 d.	6 m. 12 d.	6 m. 16 d.	6 m. 21 d.	6 m. 25 d.
Weight	5.800 kg.	5.800 kg.	6.750 kg.	6.900 kg.	6.500 kg.
Diet	3 M + 1 B 225 cc. \times 3 G. 225 gm \times 2	3 M + 1 B 225 cc. \times 3 G. 225 mg. \times 2	3 M + 1 B 225 cc. \times 3 G 225 gm. \times 2	Same diet	3 M + 1 B 225 cc. \times 3 G 225 gm. \times 2
Fasting period	6 hours	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	2 min.	2 min.
Fasting bl. s. %	0.079	0.070	0.096	0.086	0.102
0 Min.	0.089	0.091	0.092	0.089	0.105
5 »			0.148	0.115	0.144
10 »	0.138	0.140	0.177	0.138	
15 »			0.181	0.138	0.170
20 »	0.165	0.154	0.191	0.140	—
25 »			0.184	0.136	0.201
30 »	0.173	0.169	0.181	0.125	—
35 »			0.184	0.122	0.170
40 »	0.153	0.162	0.179	0.120	0.186
45 »			0.177	0.113	0.161
50 »	0.147	0.165	0.177	0.115	0.162
55 »			0.177	0.113	0.159
60 »	0.146	0.162	0.179	0.110	0.162
65 »					0.123
70 »	0.140	0.151	0.163	0.113	0.114
75 »					—
80 »	0.122	0.140	0.123	0.108	0.109
85 »					0.109
90 »	0.119	0.121	0.092	0.106	0.102
100 »	0.115	0.109	0.101	0.110	0.109
110 »	0.119	0.096	0.077	0.108	0.092
120 »	0.093	0.085	0.066	0.090	0.095
130 »	0.091	0.083	0.066	0.063	0.106
140 »	0.084	0.098	0.072	0.053	0.094
150 »	0.085	0.096	0.081	0.058	0.097

Rickets.

No. 4 (female)			No. 5 (male)
Date	Feb. 8, 1930	Feb. 13, 1930	Feb. 14, 1930
Age	7 m. 22 d.	7 m. 27 d.	7 m. 13 d.
Weight	7.160 kg.	6.830 kg.	7.500 kg.
Diet	3 M + 1 B 225 cc. \times 3 G 225 gm. \times 2	Same diet	3 m. + 1 B 225 cc. \times 3 G 225 gm. \times 2
Fasting period	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.
Fasting bl. s. %	0.057	0.059	0.076
0 Min.	0.061	0.081	0.085
5 "	0.079	0.095	0.103
10 "	0.083	0.104	0.111
15 "	0.101	0.109	0.132
20 "	0.111		0.145
25 "	0.115	0.119	0.150
30 "	0.120	0.135	
35 "	0.131	0.151	0.179
40 "	0.136	0.151	0.185
45 "	0.149	0.155	0.165
50 "	0.145	0.160	0.185
55 "	0.145	0.167	0.163
60 "	0.138	0.166	0.158
65 "	0.125		
70 "	0.117	0.158	0.131
75 "	0.108		
80 "	0.103	0.130	0.099
85 "	0.094		
90 "	0.094	0.089	0.088
100 "	0.079	0.077	0.085
110 "	0.070	0.073	0.079
120 "	0.067	0.086	0.069
130 "	0.061	0.078	0.065
140 "	0.067	0.073	0.060
150 "	0.063	0.051	0.058

Tetany.

No. 1 (female)					No. 2 (male)	
Date	Jan. 10, 29	Jan. 11, 29	Feb. 8, 29	Feb. 16, 29	Feb. 22, 30	Feb. 24, 30
Age	6 months	6 m. 1 d.	6 m. 28 d.	7 m. 6 d.	8 m. 20 d.	8 m. 22 d.
Weight	7.150 kg.	7.150 kg.	6.900 kg.	7.000 kg.	9.050 kg.	8.900 kg.
Symptoms	present	present	absent	absent	present	present
Diet	B 150 cc. × 7	B 150 cc. × 7	M 200 cc. × 2 G 200 gm. × 2 Omg. 250 gm.	Same diet	Oatmeal gruel 200 gm. × 5	Same diet
Fasting period	6 hours	6 hours	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	2 min.	2 min.	2 min.
Fasting bl. s. %	0.045	0.063	0.090	0.069	0.077	0.074
0 Min.	0.054	0.067	0.108	0.086	0.076	0.104
5 »	0.070	0.083		0.112		
10 »	0.135	0.120	0.108	0.130	0.103	0.130
15 »		0.126	0.115	0.144		
20 »	0.153	0.142	0.132	0.130	0.090	0.109
25 »	0.164	0.152	0.149	0.144		
30 »	0.179	0.169	0.143	0.144	0.101	0.093
35 »	0.182	0.170		0.140		
40 »	0.184	0.174	0.134	0.144	0.111	0.096
45 »		0.170	0.129	0.142		
50 »	0.180	0.172		0.142	0.113	0.100
55 »	0.175	0.167	0.105	0.144		
60 »	0.159	0.136	0.092	0.126	0.096	0.105
65 »	0.171	0.136	0.092	0.123		
70 »	0.146	0.110	0.092	0.116	0.101	0.119
75 »	0.143		0.094	0.100		
80 »	0.135	0.071		0.075	0.092	0.105
85 »	0.132	0.081	0.099	0.060		
90 »	0.116	0.058	0.085	0.069	0.113	0.084
105 »	0.097	0.058		0.069	0.120	0.069
110 »	0.093	0.056		0.077	0.117	0.073
120 »	0.082	0.049	0.078	0.069	0.099	0.060
135 »	0.075	0.038	0.094	—	0.103	0.073
140 »	0.072	0.038		0.059	0.094	0.082
150 »	0.054	0.045		0.055	0.079	0.066

Tetany.

No. 3 (male)					No.4(male)
Date	May 28, 29	May 30, 29	June 4, 29	June 8, 29	Dec. 3, 28
Age	8 m. 28 d.	9 months	9 m. 5 d.	9 m. 6 d.	9 months
Weight	7.280 kg.	7.000 kg.	7.050 kg.	6.900 kg.	7.500 kg.
Symptoms	present	present	absent	absent	present
Diet	3 M + 1 B 225 cc. × 3 G 225 gm. × 2	Same diet	Same diet	Same diet	1 M + 1 B 200 cc. × 5
Fasting period	6 hours	6 hours	6 hours	6 hours	6 hours
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	2 gm.
Time for ingestion	2 min.	2 min.	2 min.	2 min.	2 min.
Fasting bl. s. ₀	0.077	0.068	0.075	0.073	0.075
0 Min.	0.076	0.077	0.072	0.078	0.087
5 »					0.112
10 »	0.117	0.093	0.101	0.113	
15 »					0.115
20 »	0.115	0.087	0.113	0.134	0.140
25 »					
30 »	0.124	0.095	0.136	0.149	0.145
35 »					0.163
40 »	0.127	0.109	0.143	0.160	0.156
45 »					0.154
50 »	0.125	0.109	0.136	0.138	
55 »	0.117	0.105	0.132	0.138	0.149
60 »					
65 »					0.145
70 »	0.113	0.112	0.124	0.131	
75 »					0.138
80 »	0.106	0.112	0.120	0.125	0.136
85 »					
90 »	0.103	0.107	0.103	0.115	0.129
95 »					
100 »	0.097	0.096	0.090	0.110	
110 »	0.088	0.093	0.090	0.099	0.094
120 »	0.103	0.095	0.089	0.090	0.085
130 »	0.096	0.087	0.096	0.085	
140 »	0.096	0.086	0.090	0.078	0.096
150 »	0.099	0.080	0.085	0.071	0.087

Tetany.

No. 5 (female)			No. 6 (male)		
Date	May 2, 29	May, 17, 29	Jan. 13, 29	Jan. 23, 29	
Age	10 m. 12 d.	10 m. 27 d.	16 m. 17 d.	16 m. 27 d.	
Weight	8.250 kg.	7.700 kg.	9.700 kg.	9.870 kg.	
Symptoms	present	absent	present	absent	
Diet	Barley water 200 gm. \times 5	3 M + 1 B 225 cc. \times 3 G 225 gm. \times 2	Barley water 200 gm. \times 5	3 M + 1 B 250 cc. \times 5	
Fasting period	6 hours	6 hours	6 hours	6 hours	
Glucose per kg. of b. w.	2 gm.	2 gm.	2 gm.	2 gm.	
Time for ingestion	2 min.	1 min.	2 min.	2 min.	
Fasting bl. s. $\frac{g}{100}$	0.069	0.077	0.068	0.075	
0 Min.	0.073	0.079	0 Min.	0.081	0.081
5 »	0.108				
10 »	0.142	0.127			
15 »	0.140		10 »	0.116	0.148
20 »	0.149	0.161			
25 »	0.135		20 »	0.128	0.163
30 »	0.121	0.150			
35 »	0.103		30 »	0.125	0.163
40 »	0.105	0.141			
45 »	0.108		40 »	0.129	0.155
50 »	0.112	0.141			
55 »	0.128		50 »	0.137	0.155
60 »	0.142	0.143			
65 »	—	—	60 »	0.134	0.113
70 »	0.147	0.115			
75 »			70 »	0.120	0.133
80 »	0.142	0.115			
85 »			80 »	0.135	0.129
90 »	0.117	0.106			
100 »	0.049	0.090	90 »	0.116	0.113
			105 »	0.099	0.106
110 »	0.049	0.063			
120 »	0.042	0.081	120 »	0.098	0.101
130 »	0.051	0.070			
			135 »	0.082	0.109
140 »		0.088			
150 »	0.060	0.085		0.083	0.111

ABBREVIATIONS:

b. w. = Body weight.

M = Milk.

B = Barley water.

1 M + 2 B. 150 cc. \times 7, for instance, means 150 cc. of a milk and barley water mixture, in the proportion 1 : 2, given 7 times daily. If nothing else is stated, the milk mixture contains 2 % cane sugar.

Bum = Buttermilk.

G = Gruel (wheat).

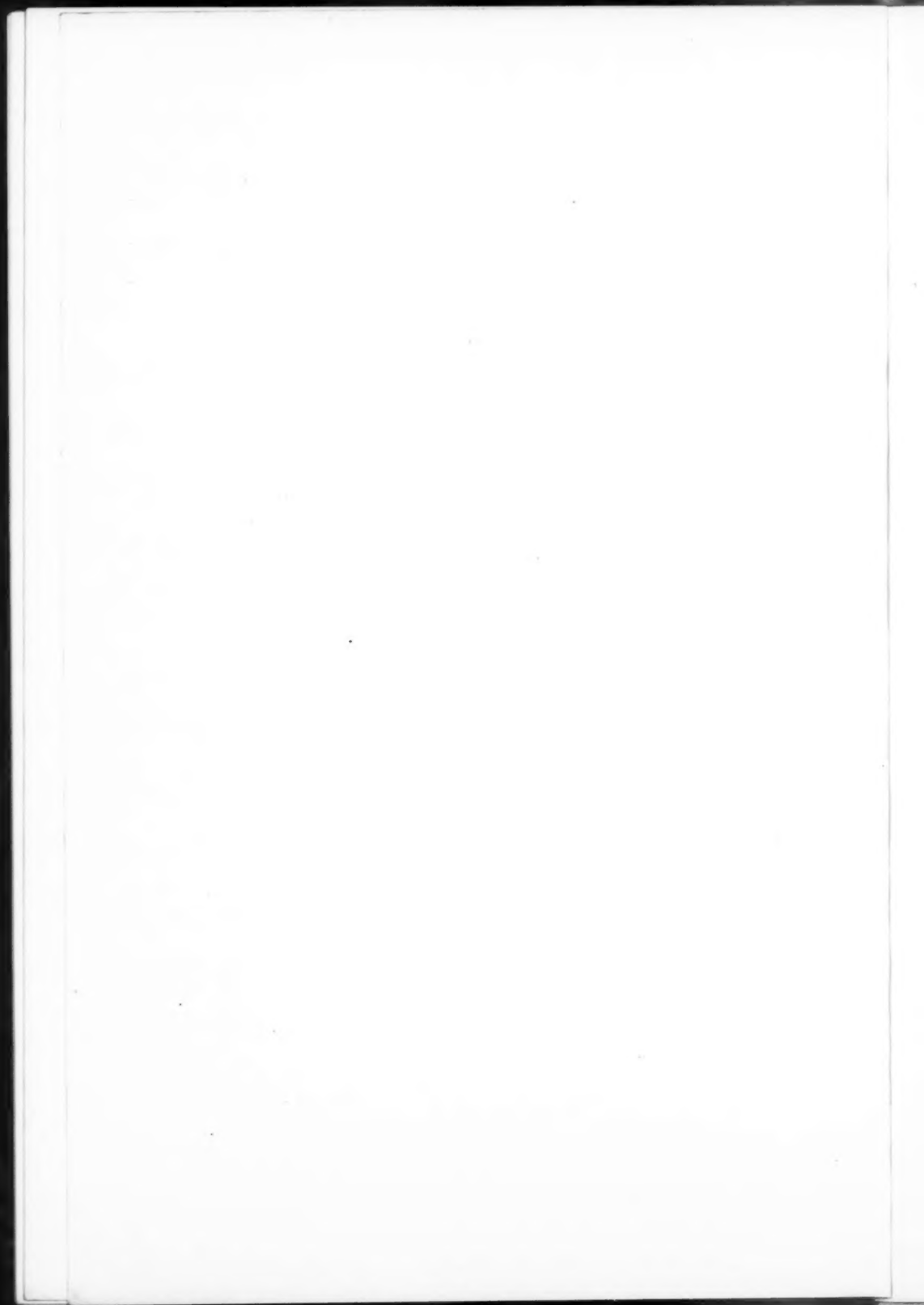
Omg = Oatmeal gruel.

bl. s. = Blood sugar.

Explanatory notes:

In the protocols, the term »*Ord. diet*« means »ordinary« diet suitable for a normal child of the age in question.

»*Time for ingestion*« means the time it takes to introduce the respective sugar solution into the stomach of the child — whether this takes place by means of a stomach tube, or the child drinks the solution.



ERRATA.

- P. 13. L. 15 f. a. 0.63, should read 0.063
P. 24. L. 14 f. a. 0.74 " " 0.074
P. 41. Under fig. 2. Preceding period, should read: Preceding
fasting period.
P. 41. Under fig. 4. months, should read: years.
P. 54. L. 9 f. b. 2 cases, should read: 3 cases
" " " " " 34 days " " 19 and 20 days
P. 56. L. 5 f. a. (No....15), " " (No....15, 19)
" " " " " 4 " " 3
" " " 6 " " 19 should be left out.
P. 92. L. 11 f. a. 19 days, should read: 45 days
P. 125. L. 8 f. a. 0.28 " " 0.028
P. 154. L. 10 f. a. 5 days " " 4 days
P. 175. L. 12 f. b. period, should be left out.